

THE ETIOLOGY OF PRIMARY PNEUMOCOCCAL PERITONITIS.

by

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Thesis for the Degree of M.D. March 1922.



I N T R O D U C T I O N .

The object of this Thesis is to show that Primary Pneumococcal Peritonitis is a disease that occurs only in female children, and that the infection reaches the peritoneum by way of the genital tract.

During the past two and a half years I have acted as Pathologist to the Royal Hospital for Sick Children, Edinburgh, and during that time I have had the opportunity of investigating a number of cases of primary pneumococcal peritonitis.

At the autopsies of the first cases, I was much impressed by the fact that no other pneumococcal lesion, other than the peritonitis, was to be found, and naturally the question arose as to how the pneumococcus gained access to the peritoneal cavity. In discussing this question with Mr John Fraser, Surgeon to the Hospital, he pointed out that all the cases he had seen were in females, and that the likely mode of infection was by the genital tract. He suggested that I should investigate the etiology of/

of the disease with a view to determining by what means the pneumococcus gained access to the peritoneal cavity.

Mr Fraser and I are publishing a paper on Primary Pneumococcal Peritonitis in the British Journal of Surgery, dealing with the subject from a clinical standpoint.

This thesis contains the results of my own investigations from clinical, bacteriological and experimental points of view.

I wish to record here my indebtedness to Mr John Fraser for his kindness in allowing me to make use of his case records, for obtaining for me at operations material for investigation, and for the interest which he showed during the course of the work.

I also wish to thank Miss Herzfeld, Assistant Surgeon to the Royal Hospital for Sick Children and also the Staff of that Institution for their assistance in obtaining material.

THE ETIOLOGY OF PRIMARY PNEUMOCOCCAL PERITONITIS.

Primary pneumococcal peritonitis is a comparatively rare disease and in a Children's Hospital is usually met with as an abdominal emergency.

It is difficult to ascertain exactly its relative incidence, but probably 2 per cent of the abdominal emergencies of childhood are due to an infection of the peritoneum by the pneumococcus.

It is a serious disease for the mortality rate is often as high as 80%, and information as to the predisposing causes is urgently required, with a view to suggesting means of prevention.

Moreover the mysterious manner of the infection of the peritoneum stimulates investigation, for with our present state of knowledge we cannot label a disease as "idiopathic" and so dismiss it. The investigation therefore of the etiology of the disease is of more than merely academic interest; it has a definite practical importance.

Pneumococcal peritonitis may be divided into two main groups, namely Primary and Secondary. In Primary cases, the only lesion found is in the peritoneum, and the first and only manifestation of the/

the disease is abdominal. The Primary focus of infection is in the peritoneal cavity.

The Secondary cases follow some pre-existing pneumococcal lesion in the body, usually in the lungs or pleura. The peritonitis is subsequent to the pulmonary lesion and is a secondary manifestation of the infection.

The Primary cases may be further subdivided into Acute and Chronic cases, so that we have three varieties of the disease, namely.-

Primary Cases (Acute
 (Chronic

Secondary Cases - usually Sub-acute.

The division between these three types of pneumococcal peritonitis is illustrated by the following clinical histories which may be regarded as typical of the three varieties of the disease.

CASE I. AN EXAMPLE OF ACUTE PRIMARY PNEUMOCOCCAL
PERITONITIS.

A female child, aged 6 years, was admitted to hospital on account of severe abdominal pain, persistent vomiting and general prostration. The illness had commenced only 24 hours before admission.

On the morning before admission the child appeared to be/

be in good health and partook of a hearty breakfast. At 10 a.m. whilst playing with a companion, she suddenly complained of severe pain in the lower part of the abdomen, and about half an hour later she vomited. She was put to bed, and throughout the day the pain continued and she vomited at intervals. These features continued during the night, and she was very restless. The next morning her condition was one of collapse with intervals of complete unconsciousness. In this condition she was admitted to hospital. On admission she was almost unconscious, and there was slight general cyanosis. Her temperature was 103°F, the pulse was uncountable and the respirations were 50 per minute. The lower half of the abdomen was rigid and did not move on respiration. Below the level of the umbilicus the percussion note was dull. In spite of her semi-consciousness, tenderness could be elicited in both iliac fossae.

An operation was performed on the same day at 2 p.m., that is 28 hours after the onset of the disease. Abdominal section revealed an intense peritonitis, most marked in the lower abdomen. From the exudate, Pneumococci were isolated in pure culture. After the operation the child became steadily worse and succumbed about 10 p.m., that is, within 36 hours of the onset of the disease.

At/

At the autopsy, the only lesion found was the peritonitis. There was no other pneumococcal focus present, either in the lungs, throat, or middle ear.

This case is characterised by its sudden onset, intense toxaemia and rapidly fatal termination.

CASE 2. A CASE OF CHRONIC PRIMARY PNEUMOCOCCAL
PERITONITIS.

Patient was a female child, aged 10 years. The illness had extended over a period of three weeks before admission to the Hospital. Its onset was marked by colic-like pains in the lower part of the abdomen, followed shortly afterwards by diarrhoea and attacks of vomiting. These three symptoms continued during the first week of the illness, but were not of such severity as to keep the child confined entirely to her bed. During the second week of the illness the symptoms continued, the pain was still severe but the diarrhoea and vomiting became less marked. She was now confined to bed on account of bodily weakness and loss of flesh. At the commencement of the third week the diarrhoea had disappeared, but there was now frequent and painful micturition, and/

and also recurrent attacks of colic. The doctor noticed the lower abdomen to be swollen and tender. The child was admitted to hospital exactly three weeks after the onset of the illness. She was a thin emaciated girl and had a general appearance of extreme nervous irritability. The mouth and lips were dry, the temperature was 102°F , and the pulse rate 120. Examination of the abdomen showed a rounded tender swelling below the umbilicus. There was a leucocytosis of 20,000 per c.m., the polymorphs showing a well marked glycogenic reaction. Laparotomy revealed the presence of an encysted abscess in the pelvis and lower abdomen. Bacteriological examination of the pus showed pneumococci to be present in pure culture.

The main features of this case are.-

1. The long history of three weeks.
2. The disease never showed acute symptoms at any stage of the history but had remained mild from its commencement.
3. The gradual formation of an encysted abdomino-pelvic abscess.

CASE 3. EXAMPLE OF SECONDARY PNEUMOCOCCAL
PERITONITIS.

Patient was a male child, aged 1 year 8 months. A month before admission to hospital, the child had an attack of bronchitis followed by pneumonia. After 3 weeks serious illness the child appeared to be well on his way to recovery. For three days he had been able to be carried out of doors and he was improving rapidly when he began to complain of pain which he referred to the left upper quadrant of the abdomen. His temperature rose, general malaise developed and there was vomiting. Jaundice was also present to a slight degree. On admission to Hospital, the child displayed the features associated with a general peritonitis. The abdominal rigidity was most marked on the left side, and the various evidences of inflammation were more pronounced in the upper than in the lower part of the abdomen.

Laparotomy showed the presence of a sub-acute pneumococcal peritonitis, most marked in the upper left quadrant of the abdomen.

THE VARIETIES OF THE DISEASE.

The above case histories are illustrative of three distinct types of the disease.

In the first two cases, the symptoms of peritonitis are the first manifestations of the disease, the patient being perfectly healthy up to the time of onset.

Neither clinically nor at autopsy is there any evidence of preceding or introductory pneumococcal infection in any other part of the body, and the primary focus of infection is in the peritoneum itself. This constitutes the Primary type and according to the severity of the infection, may be acute or chronic.

In the third case history there is definite pneumococcal lesion in the chest and the peritonitis resulted from this infection. The abdominal lesion does not dominate the clinical picture as it is only a complication of the pulmonary infection.

This essential difference between Primary and Secondary cases is important, because it is here emphasised that this Thesis deals with the consideration of the Primary cases only, as the Primary and Secondary cases have been frequently confused.

PRIMARY PNEUMOCOCCAL PERITONITIS.

HISTORICAL. Da Bozzolo (1885) first described pneumococcal peritonitis in 1885, when, examining post-mortem the pus from a case of peritonitis, he demonstrated capsulated pneumococci to be present in the exudate.

Since that time numerous observers have recorded cases and some have attempted to explain the etiology of the disease. The fact that the peritonitis exists without any other lesion being present, has puzzled not a few, and they have recorded the cases giving a few clinical details and making no attempt to explain the etiology. Others have formulated theories as to the path of infection, and have attempted to show, very unconvincingly, that their explanation is correct.

In spite of the mass of literature which has accumulated on the subject, there are few papers worthy of consideration. I have consulted a large number of references, and many papers unobtainable by me have been referred to by the authors consulted, but, in the literature up to date, no theory as to the path of infection has been proved, and the impression gained after considering all these references is that the etiology is still obscure and the views on it conflicting.

As this paper is concerned primarily with the etiology of primary pneumococcal peritonitis, only those papers referring to, or throwing some light upon the question of etiology will be referred to. It is felt that it would be unprofitable and tedious to review here all the literature consulted.

Nelaton (1890) was the first to operate on the condition and Sevestre (1890) also recorded a case operated on which recovered. This case appears to be a primary case and occurred in a "little girl".

Gaillard (1890) records a primary case in a girl aged 11 years. In discussing the etiology he emphasises three points.--

1. Traumatism.
2. "A slight vulvo-vaginitis such as is common amongst a large number of girls".
3. There was nothing to indicate the mode of infection in the post-mortem findings.

Michaut (1901) in his Thèse de Paris, gave a very good clinical account of the disease. He emphasised the differences between primary and secondary cases.

Michaut was the first to discuss the method of infection of the peritoneum and put forward the view that/

that the infection occurs by the blood stream and this is the universal path of infection in all cases of peritonitis whether primary or secondary. He thought this to be the case because "the pneumococcus readily gains access to the blood stream and can often be isolated from the blood stream in pneumonia".

Brun (1901) noticed that female children were more liable to be attacked than boys. He thought that the infection reached the peritoneum by the genital tract but was unable to bring forward any further evidence in favour of his theory.

Bryant (1901) records three fatal cases of which two are primary cases, in girls aged 5 and 8 years, and one, a secondary case, in an adult man.

Bryant, following Michaut, distinguishes between primary and secondary cases, and lays emphasis on the absence of any pneumococcal focus (other than the peritoneal) as being characteristic of primary pneumococcal peritonitis. He lays stress on the sudden onset of the disease in healthy children, and on the fact that pain, diarrhoea, and vomiting are important symptoms.

In discussing the etiology of the disease, Bryant dismisses a blood infection as improbable, but thinks infection might occur by the genital tract. He points out that the majority of cases are in girls/

girls and that the inflammation is most severe in the pelvis, and also that gonococcal peritonitis may occur as an extension from a vaginal lesion.

As no naked-eye change was noticed in the genital route at autopsy, he is unwilling to accept this theory of infection.

In summing up the various possibilities, Bryant thinks that the intestinal route is the main path of entry of the organism, but that a genital infection may occur.

- (1) Hagenbach - Burckhart records two primary cases, both in girls aged 2 and 6 years.
- (2) Audion records two similar cases also in young girls aged $2\frac{1}{2}$ and 3 years.
- (3) Quehart had 25 primary cases out of a total of 33 cases of pneumococcal peritonitis.

All the 25 primary cases were in young girls.

- (4) Boulay found pneumococci in the cavity and walls of the uterus in a primary case, and thought organisms might reach the peritoneum by this route.

(This observation is of no significance as the child died of Septicaemia, and organisms could be isolated from any part of the body.)

Stoos (1902) gave a good account of the disease in a paper which was abstracted by Fowler (1903). Stoos records 4 cases of his own. He does not distinguish between primary and secondary cases, but from the clinical histories they are evidently two primary chronic cases in girls aged $11\frac{1}{2}$ and $3\frac{1}{2}$ years, one primary acute case in a girl aged 12 years, and one secondary case in a boy aged 15, following pneumonia and acute nephritis.

In discussing the mode of infection, Stoos considers that the intestine is the source of the peritoneal invasion. He quotes the observation of Flexner (1895) who demonstrated pneumococci passing through the necrosed Peyer's patches in a case of gastro-enteritis, and lying beneath the peritoneal coat and even in the flakes of lymph exuded on the surface of the bowel. He also says "The well known fact that the wall of the bowel may, as the result of some slight lesion, allow organisms to pass through, taken along with the clinical fact that diarrhoea is often the initial symptom of pneumococcal peritonitis points to the intestine as being the most probable source of infection."

Stoos also discusses the genital route of infection and dismisses it as unlikely. He points out that/

that most cases occur in girls and that the pus is often localised in the lower part of the abdomen; but says that the examination of the genital tract at the bedside and at post-mortem has failed to lend any support to the idea that infection takes place in this manner. He says moreover that while vulvo-vaginitis is common among these cases, the uterus and tubes have been found normal.

In discussing the etiology of the disease, he refers to Michaut's theory that infection of the peritoneum is always by the blood stream. Stoos thinks that although pneumococci easily enter the circulation, they very quickly lose their virulence, and that is why only a very few cases of pneumonia are accompanied by extra-pulmonary lesions.

Stoos lays emphasis on chemical, physical and mechanical lesions of the intestine as being the main predisposing causes of pneumococcal peritonitis, and thus favour the theory of the intestinal route of infection.

Jensen (1903) gave a very good account of the disease, particularly from the clinical standpoint. He divided the cases into "Primary and Secondary". He further distinguished between the "Diffuse" and the "Circumscribed" forms of the disease.

He/

He points out the great frequency of the disease in young female children, 51 girls and 8 boys in his complete series, and lays emphasis on the main clinical points.

The interest in the paper lies in the attempt to explain the mode of infection of the Primary cases, and also in some experimental work to support his own view.

Six possible means of infection are given.-

- (1) Through the abdominal wall.
- (2) From the pleura through the diaphragm.
- (3) By the blood stream.
- (4) By the genital organs.
- (5) From the intestinal canal.
- (6) From one or other abdominal organ.

Infection through the abdominal wall he admits is rare, and quotes a case in the literature where pneumococcal peritonitis followed an operation for inguinal hernia. He thinks infection from the pleura to the peritoneum is uncommon, and in support of this view draws attention to the comparative infrequency of peritonitis complicating the large number of cases of empyema.

Jensen does not think infection by the blood stream/

stream is at all likely, although he points out that this is the view held by many French authors.

The fact that pneumococci can be isolated from the blood in many cases of pneumonia seems to him to militate against the infection of the peritoneum being haematogenous in origin.

Infection via the genital organs of course could only occur in females, and he adduces the preponderance of girls in his cases as lending some support to the view. He does not entertain this theory however, because many of his cases did not show vulvitis or vaginitis, and at autopsy the uterus was found to be healthy. He quotes the case of a 23 year old seamstress, who developed pneumococcal peritonitis and septicaemia after a self induced instrumental abortion, and thinks that the infection reached the peritoneum by way of the Fallopian tubes. He suggests that not only the streptococcus, but the pneumococcus may cause puerperal fever. He also mentions the observation of Canon (1893) who recorded a case of carcinoma of the uterus and vagina, in which pneumococcal peritonitis was a complication. Summing up however, Jensen concludes there is no evidence in favour of the genital route of infection.

Jensen himself thinks that infection from the intestinal/

intestinal canal is responsible for the peritonitis.

He points out that pneumococci may be present in the faeces, and as pneumococci are almost invariably present in the mouth and are swallowed, this is not surprising.

He thinks that the statement that pneumococci are killed off in the gastric juice is inaccurate, and that many organisms reach the intestinal canal and may cause infection there. He quotes cases, most by other writers but some of his own, in which pneumococci have been found (along with other organisms) in the exudate in peritonitis. In all these cases however, the peritonitis followed some definite lesion of the bowel such as gastric ulcer, perforated duodenal ulcer, acute obstruction, gangrene, perforative appendicitis, and tuberculous ulceration.

No case was quoted in which there was an absence of any previous lesion of the intestinal tract.

He also quotes the case of a boy aged two months, suffering from severe membranous enteritis, which was followed later by pneumococcal peritonitis.

In another case there were numerous ulcerations of the colon followed by general peritonitis, and among the many organisms found in the peritoneal exudate was the pneumococcus.

Jensen was able to isolate pneumococci from the intestine/

intestine in certain cases, in one instance from an adult male suffering from croupous pneumonia. He thinks that the presence of pneumococci in the intestinal canal has a great significance.

Lastly. He emphasises that the symptoms are mainly intestinal, colic and pain, and although vomiting may soon cease in the history of a case, the diarrhoea may continue, and the stools may contain mucus.

He concludes therefore that any intestinal lesion, from slight obstruction to gangrene, may allow organisms to pass through the intestinal wall. He finishes his remarks by lamely stating that he does not understand why pneumococci do pass through the slightly injured intestinal wall, but thinks that it is either due to a higher virulence or lowered resistance. All these he says are but hypotheses and expressions of ignorance.

The clinical evidence brought forward by Jensen in support of his view, is very unconvincing and equally doubtful is the experimental evidence he gave.

Jensen fed guinea pigs with virulent cultures of pneumococci and in one instance produced pneumococcal peritonitis.

He/

He himself states that the peritonitis was a terminal phenomenon and occurred later in the disease, and was a result of the direct extension by the pneumococcus through the very inflamed wall. Moreover the Peyer's patches were necrotic.

This is only a single experiment and has no parallel with the appearance of the intestine in human cases.

Jensen was the first to show that pneumococci injected into the peritoneal cavity of guinea-pigs and rabbits could be detected within a few minutes in the blood stream.

Von Brunn (1903) in a long article gives details of 56 cases from the literature. Of these only 7 cases were in boys, and from the description given, were obviously secondary cases.

Von Brunn concludes that the infection reaches the peritoneum by the blood stream and supposes that that peritoneum is specially sensitive in the cases which contract the disease.

Dudgeon and Sargent (1905) record a case of primary pneumococcal peritonitis in a girl aged 6 years, where death occurred within 48 hours of the onset. At autopsy a drachm of pus was found in the uterus.

Annand and Bowen (1906) give a good clinical account of the disease from a study of 45 cases. They/

They think the infection is from the intestine on account of the abdominal pain and the diarrhoea. They also draw attention to the high proportion of females and explain this by saying that the disease is not properly recognised and if all cases could be examined the proportion of boys to girls would be equal.

At autopsy two cases showed congestion of the Fallopian tubes.

Ashdowne (1906) records a case in a married woman, age 29 years, but from his description it is not at all clear if it is a true primary case. He thinks that the genital path of infection is probable, and quotes Michaut's total of 33 cases, of which 27 cases were in girls. He also quotes Lop, who records a case of pneumococcal peritonitis following delivery, in which pneumococci were present in the lochia.

Ashdowne could only collect 36 cases of the disease in adults in the literature up to 1906.

Rischbieth (1910) gave a comprehensive review of the disease based on a study of 57 cases (both primary and secondary), occurring in children.

He denies the existence of primary pneumococcal peritonitis, but says that all cases are secondary to lesions elsewhere in the body, the organisms being carried/

carried to the peritoneum by the blood stream.

He says.- "The term "primary", in whatever of several senses it may conceivably be employed, is inaccurate when applied to pneumococcal peritonitis. Thus, whether the term is used because no original diseased focus, (appendix, Fallopian tube, etc.) is ever found on operation, or is applied to cases in which there is no present evidence of pneumonia, or to imply that pneumococcal peritonitis occurs without other lesions, it is equally inaccurate. Pneumococcal peritonitis like all other varieties of general peritonitis, is always secondary, but not to a single focus of disease as in that following appendicitis, but to septicaemia. The view that the condition is secondary to pneumococcal septicaemia is the only one which is capable of explaining all cases."

He further states.- "There is no evidence for the view that infection takes place by way of the genital tract, nor that it occurs by direct spread through the diaphragm, or from the gastro-intestinal tract."

Rischbieth states that pneumococcal peritonitis is rare in adults, occurring usually as a complication to pneumonia. He has only seen one case (in a male) occurring as a complication in 6000 cases of pneumonia.

He/

He thinks defective hygiene, especially overcrowding, is a predisposing influence in the causation of the disease.

In order to explain the lesion being confined to the peritoneum, Rischbieth assumes that there is a local susceptibility. Moreover he thinks that there are several strains of pneumococci, each strain responsible for one infection only, thus one strain only produces pneumonia, and another strain only produces arthritis, etc.

With regard to the mode of infection Rischbieth gives the same possibilities as Jensen.

With regard to infection by the genital tract, he says that this method is of course only possible in girls. He points out that there are no symptoms of pyosalpinx in the female and with regard to vaginitis he says "The presence of vaginal discharge in cases of pneumococcal peritonitis is of no consequence."

He does not think the infection is from the intestinal tract because there is no evidence in favour of it.

Rischbeith lays stress on the occurrence of pain before vomiting and diarrhoea, because if the infection had been primarily in the intestinal mucous/

mucous membrane, the diarrhoea would have commenced the illness.

He also states that there is no evidence of spread of infection from the pleura by the diaphragm. His arguments are too involved and his statements too inaccurate for further consideration.

With regard to the morbid anatomy of the disease, Rischbieth only examined the uterus, vagina and Fallopian tubes macroscopically. The description is too meagre, and his observations too incomplete for his conclusions to be of any value.

The clinical description of the disease is good, but as he has not divided his cases into primary and secondary groups, the arrangement is chaotic and confusing.

Woolsey (1911) discusses the etiology at some length and favours the intestinal route of infection. He thinks that the disease is more common in girls because they do not expectorate freely like the males, but swallow their sputum. Any gastric disturbance would allow the pneumococci to pass into the intestine. He also mentions that the infection occurs mostly in females, (All his cases were females) but says "there is singularly little pathological proof of the genitals being the common channels of infection."

Salzer/

Salzer (1912) gives an account of 11 cases all in young girls.

With regard to the clinical recognition of the disease he emphasises the fact that abdominal pain is the first symptom.

He discusses the etiology and points out that there is no unanimity as to the source of the infection, some observers supporting the haematogenic and others the intestinal theory.

Although admitting that practically all cases are in young girls, he cannot agree with the view of Riedel, who suggested that infection is by the genital tract, because in none of his cases could he isolate pneumococci either from the internal or external genital organs.

Stone (1912) records a typical primary case in a girl aged 5 years.

The pain was most intense below the umbilicus, and diarrhoea was a marked symptom in the disease. There was a vaginal discharge which contained gonococci, but no mention was made as to the presence of pneumococci in the discharge. At operation, no intestinal or genital lesions could be found. Death ensued but there was no autopsy.

Moro (1917) at a Meeting of Surgeons, who were discussing peritonitis, thought that in Primary Pneumococcal/

Pneumococcal Peritonitis, the infection reached the peritoneum by the blood stream. His arguments in favour of this view were not very convincing.

Menge at the same meeting supported the opinion of Moro, but Wilms thought the infection came through the bowel wall from the intestinal canal.

Lambert (1918), at a meeting of American Surgeons gave an account of primary cases in young girls. He quoted a case which supports the view that infection is by the genital tract. A man developed pneumonia due to a Type I pneumococcus. His daughter who nursed him developed pneumococcal peritonitis, and blood culture showed the presence of pneumococcus Type I. The nurse who looked after the daughter also developed pneumococcal peritonitis due to Type I organism. In the child the disease was diffuse; in the nurse it was localised.

At the discussion, Lilienthal of New York thought the infection was by the genital tract in the female. He himself had never seen a case in a boy.

Whipple, at the same meeting said that he had 7 cases which had been examined bacteriologically. In 4 cases the pneumococci were typed, 3 being of Type I and one of Type IV. Two of the Type I cases were treated with the appropriate Type Serum and recovered. The third case had no serum and died. The Type IV case had a rapid and fatal course.

DISCUSSION OF THE LITERATURE.

From the review of the literature, it is obvious that the views on the etiology of the disease are very divergent. Several facts however stand out quite clearly.

- Firstly, that primary pneumococcal peritonitis affects mostly young girls at ages from 3 to 7 years.
- Secondly, that the disease is very rare in adults.
- Thirdly, the infection commences in the lower part of the abdomen.
- Fourthly, that no writer has proved satisfactorily that the mode of infection is either by the blood stream, by the intestinal canal, or by the genital tract.

I have carefully examined the clinical histories of the cases when recorded, and no undoubted case of primary pneumococcal peritonitis occurring in a male has been clinically described in the literature.

Jensen, Stoos and Rischbieth all record they had a few cases in boys but give no case history or details of any case. They described primary cases in detail, but these were all in girls. Autopsies were only performed in a very few cases, and the bacteriology seldom/

seldom worked out; (Rischbieth for example, diagnosed some of his cases without even examining the pus microscopically). Not too much reliance therefore can be placed on the relative sex incidence of primary pneumococcal peritonitis, on account of the incompleteness of many of the examinations.

In the numerous papers consulted I have been unable to find a description of a case in a boy which was an undoubted primary case of the disease.

If we assume the view that infection is by the blood stream, there are many points which are difficult, if not impossible, to explain. It is a generally accepted fact that the pelvic peritoneum is much more resistant to infection than the peritoneum elsewhere in the abdominal cavity. The principle of "Fowler's position" depends on this fact. Why then should the pneumococcus, if it be blood borne, pick out the most resistant portion of the peritoneum? Why should the infection affect almost invariably girls? Why does not the disease affect adults? These facts cannot be satisfactorily explained by the haematogenic theory.

Rischbieth, who is the most ardent supporter of the haematogenic theory, holds that all pneumococcal diseases are primarily due to a septicaemia (or more strictly correct, a bacteriaemia). In support of his/

his view he points out that pneumonia has a haematogenic origin, being produced by organisms conveyed to the lung by the blood stream. This conception is apparently founded on the fact that the pneumococcus can be shown to be present in the blood at the time of onset of clinical symptoms of pneumonia, or in occasional instances, before the clinical symptoms have appeared. In point of fact however, pneumococci can be obtained from the blood in practically every case of pneumonia. This haematogenic view of the cause of pneumonia has been definitely disproved by the recent work of Blake and Cecil (1920).

These observers showed that it was only by intra-tracheal injection of pneumococci, that lobar pneumonia could be produced in monkeys, and that a quantity, as small as a millionth of a cubic centimetre of a broth culture was sufficient always to induce a severe or fatal case of the disease. Under these conditions it was found that organisms appeared in the blood stream within 6 to 24 hours after the intra-tracheal injection, frequently before clinical evidence of pneumonia or elevation of temperature had developed.

Moreover Blake and Cecil showed that by intravenous injection of pneumococci a fatal septicaemia was produced, but in no case did either pneumonia or peritonitis occur.

As pneumococci gain access to the blood stream in practically every case of pneumonia, one would expect that pneumococcal peritonitis would be a very common complication of pneumonia if Rischbieth's view were correct. Actually, peritonitis is a rare sequel to pneumonia. Rischbieth himself admits this fact, and records that in 6000 cases of pneumonia only one case developed peritonitis. Rolleston's figures are 11 cases of peritonitis in 4454 cases of pneumonia or .24%.

Surely there would be a bigger percentage than this if peritonitis were caused by blood infection.

Moreover in these 11 cases, the probability is that there will be certain of them in which the infection was conveyed from the pleura, through the diaphragm by lymphatics to the peritoneum, which would still further reduce the number of cases which could have been due to the organism being carried by the blood stream.

Furthermore, (quoting Rischbieth's own figures) in 6000 cases of pneumonia where we have a definite pneumococcal focus and where we know pneumococci were circulating in the blood stream, only one case of peritonitis occurred; yet we are asked to believe that the blood stream is the route of infection even/

even in cases where no such pneumococcal focus can be demonstrated to permit of organisms gaining access to the circulation.

From a general consideration therefore, it is most improbable that the haematogenous theory is the correct one. The view that the infection is from the gastro-intestinal tract is open to the same criticisms as the foregoing theory. The sex incidence, and the age incidence of the disease render this view improbable.

As the pneumococci which may be swallowed with the sputum can, under certain conditions survive the action of the gastric juice, then a peritonitis would be one of the commonest complications of pneumonia instead of one of the rarest, as in this disease much sputum is swallowed, and gastro-intestinal disturbances are frequent.

There is no record in the literature of any gastro-intestinal lesions having been found at autopsy in a true primary case of the disease, which could account for the pneumococcus passing through the intestinal wall.

Lastly, Jensen's experiments are very inconclusive as he himself admits. If the disease is really due to an infection passing through the intestinal wall, then the feeding of animals, highly susceptible/

susceptible to the pneumococcus, such as the rabbit, should be able to reproduce the disease.

From a consideration therefore of the clinical and experimental evidence recorded in the literature it would seem unlikely that the pneumococcus reaches the peritoneum through the intestinal wall.

The view that the infection is by the genital tract has hitherto received no serious consideration. It is obvious that this route of infection must be confined to the female sex. From the preponderance of female cases, many observers have thought this route possible, but have hesitated to commit themselves definitely to any opinion. The absence of any gross lesion in the Fallopian tubes, and the absence of any obvious vaginal inflammation have led other observers to think this method of infection as unlikely.

As far as can be ascertained, no experimental work has been done on the subject, and no serious attempt has been made either to prove or disprove the correction of the theory of infection.

In favour of the genital route of infection we have.-

- (1) All the proved primary cases of the disease have occurred only in girls.
- (2) There is a direct communication from the vulva to the peritoneal cavity in the female.
- (3)/

- (3) If the pneumococcus can get directly into the peritoneal cavity without having to pass through tissue, then no other pneumococcal lesion will be found and this is in accordance with the recorded facts of the disease.
- (4) The sudden entry of the pneumococcus into the lower part of the abdominal cavity, would explain the disease occurring suddenly in an apparently healthy person, and also that the location of the disease is sub-umbilical.

SUMMARY OF THE LITERATURE.

- (1) The most likely routes of infection in primary pneumococcal peritonitis are:-
 - (a) by the blood stream.
 - (b) from the intestinal canal through the bowel wall.
 - (c) by the genital tract in the female.
- (2) Infection by the blood stream and from the intestinal canal seem unlikely, and neither of these theories are in accordance with the clinical facts of the disease.
- (3) Infection by the genital tract has been neither proved nor disproved. This view has not had the serious consideration it deserves. There is much recorded evidence in favour of such a route of infection.

MATERIAL EMPLOYED IN THIS INVESTIGATION.

From a consideration of the literature it seemed probable that the mode of infection of the primary cases of the disease was by the genital tract.

I decided to approach the problem from several points of view, namely clinical, bacteriological and experimental.

The material used in this investigation consisted of.-

- (1) Clinical Study of the case histories of 72 cases of pneumococcal peritonitis of which 36 were primary cases.
 - (2) A complete bacteriological examination of 10 primary cases.
 - (3) A pathological study of the three fatal cases in which permission to perform an autopsy was obtained.
 - (4) A study of the vaginal flora and vaginal reaction in children.
 - (5) Animal experiments.
-

CLINICAL STUDY OF CASES OF PNEUMOCOCCAL PERITONITIS
ADMITTED TO THE ROYAL HOSPITAL FOR SICK CHILDREN,
EDINBURGH.

The case histories of 72 cases of pneumococcal peritonitis have been studied and of these 53 were in females and 19 were in males. In every male case, without exception, there was a definite history of preceding pulmonary infection. The chest lesion varied, - bronchitis with bronchopneumonia, lobar pneumonia, pleurisy and empyema. In this series of cases there was not a single case of primary pneumococcal peritonitis recorded in a boy. Every male case was secondary to a chest lesion. Of the females, there were 36 primary cases and 17 secondary cases, so that the proportion of boys to girls in secondary cases is almost equal.

Briefly therefore, in 72 cases of pneumococcal peritonitis 36 cases or 50% were primary cases and all occurred in the female sex. Not a single case occurred in a boy, and of the secondary cases, the proportion of boys to girls was almost equal.

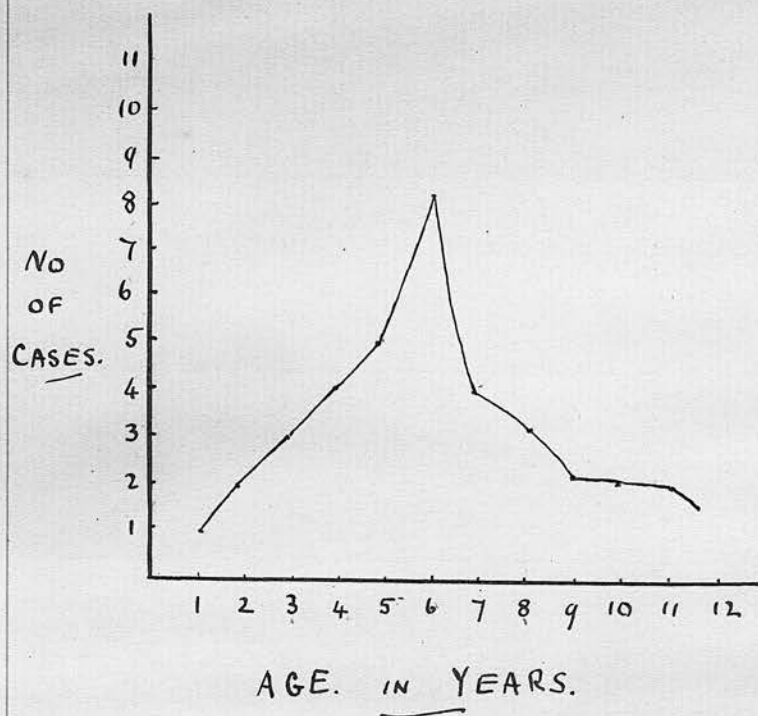
ANALYSIS/

ANALYSIS OF THE 36 PRIMARY CASES.

AGE INCIDENCE. As the age limit for admission to the Hospital is 12 years, no statistics can be given of cases above that age.

The following chart shows clearly the age incidence of primary cases of the disease. In compiling this chart, the age is given to the nearest whole year, thus 5 years 4 months is put down as 5 years, while 3 years 7 months and 4 years 3 months would both be counted as 4 years.

CHART SHOWING AGE INCIDENCE.

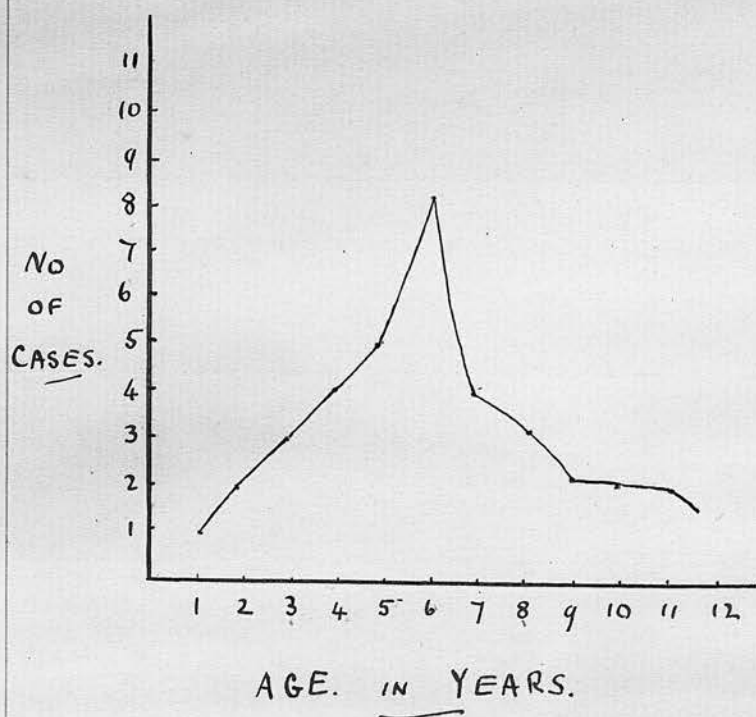


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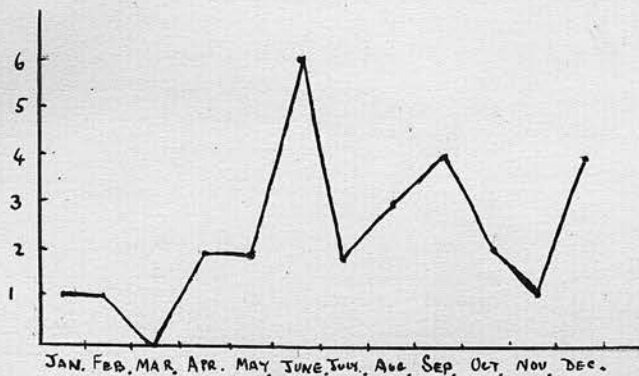
The case during the first year of life is a doubtful one.

From the above chart it is seen that 27 cases of the 36 cases occurred between the ages of 3 and 8 years, the maximum number being in the 5th and 6th years.

The preponderance of cases at this age is also seen in a study of the recorded cases in the literature. This distinctive age incidence will be discussed later and the possible explanation for its occurrence given.

SEASONAL INCIDENCE. The seasonal incidence was studied in 27 primary cases occurring between December 1918 and January 1922. It is thus seen that there are 4 winters and 3 summers in this period.

CHART SHOWING SEASONAL INCIDENCE.



It would appear that most of the cases occur in the summer months, and the seasonal incidence does not follow that of pneumonia, in which disease the cases are most numerous in the Winter and Spring months. (Osler). Primary pneumococcal peritonitis therefore has its highest incidence in the summer months when the incidence from respiratory pneumococcal affections is at its lowest.

SOCIAL CONDITIONS. Primary Pneumococcal Peritonitis is essentially a hospital disease of the lowest classes. It is

not recognised by the general practitioner who sends in the acute cases as "appendicitis" or the chronic ones as "tuberculous peritonitis". He sees very few cases even in the course of a lifetime, and the condition is often not recognised until the abdomen is opened. All the cases studied here have been in the lower classes where the child was uncared for and where the personal hygiene was neglected.

As far as can be ascertained by enquiries, the disease is unknown in better class families where the children wear adequate underclothing, and are properly washed and looked after. It is only the dirty and neglected child of poor parents, brought up in unhygienic surroundings who contracts the disease.

This observation is important and will be discussed later.

CLINICAL FEATURES OF THE DISEASE AND THEIR RELATION
TO THE ETIOLOGY.

According to the virulence of the organism and the resistance of the patient, so the disease may be so acute as to cause death within 24 hours or be so chronic as to be mistaken for tuberculous peritonitis. It is therefore desirable to select moderately acute types so that the clinical features are not masked by the overwhelming toxicity of the fulminating infection, or by the mildness of the chronic case. Only those clinical symptoms which have any bearing on the etiology of the disease will be discussed.

PAIN. The consideration of this symptom is important.

The disease is suddenly ushered in with an attack of pain in the lower abdomen.

The onset of the pain is sudden and occurs in healthy persons. The pain is almost invariably in the sub-umbilical region and appears to be more severe on the right side than on the left, which accounts for the disease being frequently diagnosed as appendicitis. The pain is due to a sudden contraction of the smooth muscle fibres of the intestine and probably occurs shortly after the entrance of the pneumococcus into the/

the abdomen. It is not possible to give the exact incubation period, but it is probably only a few hours.

Pain continues throughout the attack, at first localised to the lower abdomen, and later becoming generalised over the abdomen as the whole peritoneal cavity becomes infected.

VOMITING. A characteristic feature of the disease is the excessive vomiting during the early acute stage. It is sometimes so severe that some observers have suggested that it is due to the selective action of a toxin on the central nervous system. It differs from the reflex vomiting of an acute appendicitis, and moreover its occurrence very shortly after the onset of pain excludes the possibility of its being due to obstruction.

DIARRHOEA. This symptom is also characteristic of the disease. It usually occurs within a few hours after the onset of the disease, and is a common feature. It is not possible to give actual figures as to its frequency, because on account of the vomiting and pain, the child is often given an aperient by its parents.

Diarrhoea/

Diarrhoea in secondary cases is not so marked or so constant a feature as in the primary cases.

The occurrence of diarrhoea soon after the onset of the disease is regarded as being strong presumptive evidence in favour of the infection commencing as a pelvic peritonitis.

URINARY SYMPTOMS. In a proportion of the cases there was a history of frequent and painful micturition. These symptoms are regarded as being due to pelvic irritation, and support the view that the infection is pelvic in origin.

D I S C U S S I O N .

The evidence obtained from the clinical study of the cases is entirely in agreement with the theory that infection is by the genital tract.

Surely it cannot be a coincidence that all of the 36 primary cases are in girls, because when we consider the 36 secondary cases in our series the proportion of boys to girls is roughly equal.

This evidence, taken in conjunction with the evidence obtained from the literature, namely, that no undoubted/

undoubted case of primary pneumococcal has been recorded in a boy, is regarded by the writer as being of extreme importance.

If cases never occur in males but only in girls, the obvious conclusion is that the pneumococcus can reach the peritoneum by a route in the female which is not present in the male. The male peritoneal cavity has no communication with the exterior whereas the female has a direct communication by way of the Fallopian tubes, uterus and vagina. An infection of the peritoneum by the blood stream would affect both sexes equally, and the same criticism applies to the intestinal and to the lymphatic paths of infection. It cannot be imagined that the female peritoneum is so much more sensitive to infection by the pneumococcus, so that infection by the blood stream, intestine, or lymphatics is more likely to occur in girls.

Therefore, the only and obvious reason for the disease occurring in girls, is because the infection reaches the peritoneum by the genital tract.

But there are other considerations from a clinical study of the disease, which lend additional support to this view. The first consideration is that of the AGE INCIDENCE. 75% of the present series of cases occurred between the ages of 3 and

7 years. Moreover although a case of 11 months is included, the youngest undoubted case occurred at 22 months of age. Few cases occurred in older children, while the disease is exceedingly uncommon after puberty. This cannot be considered a coincidence, as the cases recorded in the literature show a similar age incidence. Why therefore should the infant and the adult be immune, while the disease chiefly affects children about the 5th year? It cannot be a question of susceptibility to the pneumococcus, as other pneumococcal infections, such as pneumonia, have no such age incidence.

The gastric and intestinal disturbances, which are said to predispose to a pneumococcal infection of the intestine, are much more common in infants than in older children. There is no history, in this series of cases, of previous intestinal disorder to account for the supposed passage of the pneumo-coccus through the bowel wall. All these cases occurred suddenly and while the patient was in perfect health, and moreover on clinical examination, no other pneumococcal focus was present to which the peritonitis could be secondary.

The case histories also show that children belong to the lower classes, in which the personal hygiene/

hygiene is very apt to be neglected. There was no case from a well-cared-for family.

Enquiries, as to the occurrence of the disease in the middle and upper classes, have shown that the disease is unknown. Surgeons with extensive practice amongst better class patients have informed me that they have never seen a case of primary pneumococcal peritonitis in well-cared-for children.

This also shows that it is a disease due to environment and not to the ordinary risks of infection.

The clinical symptoms of pain, vomiting and diarrhoea, are all compatible with an acute infection. The sudden onset of sub-umbilical pain as the first symptom shows that the peritoneum is the first tissue to be attacked. The absence of any other clinical pneumococcal lesion also shows that the primary focus of infection is peritoneal. The symptoms of diarrhoea and of frequent and painful micturition are evidence of pelvic inflammation.

The clinical evidence therefore is entirely in favour of the theory of the genital route of infection.

S U M M A R Y.

- (1) Primary Pneumococcal Peritonitis affects only girls.

(2)/

- (2) Girls of the lower classes between the ages of 3 and 12 years are most liable to contract the disease.
- (3) The infection is more common in the summer than in the winter.
- (4) The first symptoms of the disease are pain in the lower abdomen, and evidence of pelvic irritation.
- (5) Secondary pneumococcal peritonitis occurs in boys and girls in about equal proportions.

BACTERIOLOGICAL EXAMINATION OF CASES OF
PRIMARY PNEUMOCOCCAL PERITONITIS.

From a study of the literature it is very evident that this aspect of the disease has been much neglected by workers in the past. Formerly the pneumococcus was always thought to be pathogenic and the presence of pneumococci in any site was taken as being evidence of infection. From the recent work done at the Rockefeller Institute we now know that there are several groups or Types of pneumococci, and therefore it does not suffice merely to identify any organism as the pneumococcus, but in addition the Type must be ascertained. Types I and II pneumococci are always pathogenic, while Type IV is usually non-pathogenic. Therefore if pneumococci are found in different parts of the body, no conclusions can be drawn from the observations unless we take into consideration the Type of organism present. It was at first considered doubtful that the pneumococcus was the cause of pneumonia since pneumococci could be isolated from the mouths of healthy people. We now know that Types I and II pneumococci are responsible for most cases of pneumonia, whereas non-pathogenic organisms such as may normally be found/

found in the throat of a healthy individual belong to Type IV.

It therefore seemed to me that some light might be thrown on the etiology of the disease if a systematic study was made not only of the organisms from the abdominal infection, but also of pneumococci isolated from other parts of the body.

If the disease is due to infection from the vagina, then it is natural to suppose that pneumococci might be found in the vaginal secretion. Moreover pneumococci occur normally in the mouth. Are these pneumococci of the same type as the organism causing the disease? Pneumococci may be found in the blood stream in other pneumococcal infections, are they present in this disease, and, if so, at what stage of the infection?

In order therefore to investigate more fully the disease from a bacteriological standpoint, the following material was obtained in each case at operation from cases of primary pneumococcal peritonitis. In all, 10 cases were thus examined. The material obtained consisted of.-

- (1) Swab or pus taken from the upper part of the peritoneal cavity.
- (2) Swab or pus from the pouch of Douglas.
- (3)/

- (3) Swab from the vagina.
- (4) Swab from the throat.
- (5) Blood for blood culture ($\frac{1}{2}$ - 3 cc.)
- (6) Sample of urine (usually a catheter specimen).

The objects in procuring these specimens were.-

- (1) To isolate the causal organism, to prove it to be the pneumococcus and to determine its Type.
- (2) To determine if possible if the severity of the infection varied in different parts of the peritoneal cavity, with a view to ascertaining the locality in which the infection commenced.
- (3) To determine the presence or absence of the pneumococcus in the vaginal flora, and if present to determine its type.
- (4) To isolate the pneumococcus from the throat, to determine the Type for comparison with other types of pneumococci isolated from other parts of the body.
- (5) To determine whether organisms are present in the blood stream, at what stage they appear in the circulation, and also to determine the importance of a bacteriaemia on the prognosis of the case.

- (6) Investigation of the urine with regard to the presence of a "precipitin" reaction when the urine is mixed with an antipneumococcal serum.

METHODS EMPLOYED.

- (1) Film preparations were made from the abdominal pus, vaginal secretion and material from the throat, and stained by Gram's Method, Hiss's Method, and Muir's Method for capsules.
- (2) Cultures were made from the abdominal pus direct into rabbit blood broth, or on to rabbit-blood or sheep-serum agar, and a pure culture of the organism was usually obtained.
- (3) Material from the vagina and from the throat was inoculated into rabbit blood broth or serum broth, and in addition plated out on rabbit blood agar when possible; failing this sheep-serum agar was used.
- (4) When cultures from the vagina and throat were overgrown by other organisms so that isolation by plating was difficult or impossible, white mice were inoculated, either subcutaneously or intraperitoneally with the mixed culture. The pneumococcus was recovered in pure culture, and in addition the organism was shown to be virulent.

IDENTIFICATION OF THE PNEUMOCOCCUS.

It is essential to distinguish most carefully the pneumococcus from other allied organisms such as the streptococcus. This differentiation can only be done by biological methods, and has not been done by previous investigators.

In the past proper bacteriological examination has been sadly neglected, and in many cases no bacteriological examination has been done. Thus in Rischbieth's series of 24 cases, cultures were only made on 13 occasions. Other observers, finding pneumococci in the throat and intestine have concluded that these organisms must be virulent, without determining whether they belonged to a virulent type or not. Moreover there are organisms resembling both the streptococcus and the pneumococcus such as the streptococcus mucosus, and these organisms have been recognised only recently.

A complete study of the organisms isolated and their differentiation into the various types was considered absolutely essential in this investigation.

The differentiation between the pneumococcus and the streptococcus cannot definitely be made by microscopical/

microscopical examination alone. The main differences between these organisms may be summarised as follows.

The pneumococcus is bile soluble, ferments inulin, and is very pathogenic for white mice. It grows on blood agar in the form of small, flat, moist, "ringed" colonies, surrounded by a greenish zone of methaemoglobin.

The streptococcus on the other hand is not bile soluble, does not ferment inulin, and its pathogenicity for white mice is much less. On blood agar, the colonies are more opaque, definitely raised, appear drier, and are not "ringed" like those of the pneumococcus.

Streptococcal colonies are also surrounded by a zone, either of haemolysis or of green pigmentation. The most important tests for establishing the identity of the pneumococcus are:-

- (1) Bile Solubility
- (2) Agglutination of the various types of pneumococci by the homologous specific antisera.

These two tests have been the criteria for diagnosing the pneumococcus in the investigation here described.

The presence of a capsule round the organism cannot, for several reasons, be relied upon as being characteristic/



characteristic of the pneumococcus. These reasons are:-

- (1) The Streptococcus Mucosus has a capsule.
- (2) Besredka has shown that ordinary streptococci may develop capsules under certain pathological conditions, such as the intravenous injection of the organism into rabbits.
- (3) In Type IV pneumococci the presence of capsular formation is variable. In some strains it is well marked, in others it is very irregular, and at times it may be impossible to demonstrate a capsule even when the condition appears to be most favourable.

Although the fermentation of inulin in Hiss's serum water medium is not absolutely infallible, all strains isolated during this work produced acid, and coagulation of the medium.

TYPING OF THE PNEUMOCOCCI ISOLATED.

In this test the Rockefeller Institute Type Sera, (kindly obtained for me by Professor Ritchie) were used. The Rockefeller Institute Technique as described by Dochez and Avery was adhered to. This test consists in adding a broth culture of the pneumococcus/

pneumococcus to its homologous type serum, and observing the phenomenon of agglutination of the organism. Some difficulty was encountered at first in obtaining nutrient broth that would grow the pneumococcus without the addition of serum, but by carefully following the technique of the Rockefeller workers (1917) a satisfactory medium was obtained. This however is more difficult than the description by these writers would lead one to expect.

The main points to be observed are:-

- (1) The use of fresh meat.
- (2) The avoidance of excessive heating during sterilisation.
- (3) The careful adjustment of the reaction.

It is necessary to use a serum free medium, as the presence of serum in pneumococcus cultures, while not having any appreciable effect on the phenomenon of agglutination, inhibits or completely arrests the lytic action of the bile, in the bile solubility test, which is performed at the same time.

The following Table indicates the method of Determination of Pneumococcus Types by agglutination, according to the Rockefeller Institute technique. It will be observed that the organism is added to Types I, II, and III sera suitably diluted, and also to ox bile. Types I, II, and III are denoted by agglutination/

agglutination in the appropriate serum, whilst organisms which are not agglutinated by these three Type sera, and yet are shown to be pneumococci by the bile solubility test, belong to Type IV.

Types I, II, III, are pathogenic organisms, whereas the non-virulent pneumococci, such as are found in the throats of healthy persons belong to the Type IV group.

Broth Culture of Pneumo- coccus 0.5 cc	Serum I. (1-10) 0.5 cc.	Serum II. Undiluted 0.5 cc.	Serum II (1-10) 0.5 cc.	Serum III (1-5) 0.5 cc.	Bile .1 cc.
Type I.	++	-	-	-	+
" II.	-	++	++	-	+
Subgroups IIa, b, x.	-	+	-	-	+
Type III.	-	-	-	++	+
" IV.	-	-	-	-	+

Incubation 1 hour at 37°C.

Note. In the column under "Bile", "+" indicates bile solubility, and only 0.4 cc. of Pneumococcus culture is added. The bile is thus finally a diluted 1 in 5.

The dilutions of the Type Sera were indicated on the bottles received and differ from the published dilutions.

The specific precipitin reaction in the urine has been used by the Rockefeller Institute workers as a means of determining the type of pneumococcus causing infection.

It has been shown by Dochez and Avery (1916) that a certain percentage of patients suffering from lobar pneumonia excrete in their urine a soluble substance of pneumococcal origin. When the urine is mixed with an anti-pneumococcal serum, this substance gives a specific precipitin reaction corresponding in type to the organism causing the infection.

Unfortunately this precipitin reaction does not always occur, as in 111 cases of pneumonia investigated by Dochez and Avery, only 65% gave a positive reaction. When the reaction is positive however it gives information as to the type of pneumococcus present, without the trouble of isolating the organism.

No references can be found in the literature, of this test being applied in cases of pneumococcal peritonitis.

METHOD. A sample of urine (preferably a catheter specimen) is obtained, and cleared by centrifuging. The clear urine is mixed in quantities of 0.5 cc. with equal amounts of antipneumococcal serum.

The following table indicates the technique employed.

METHOD FOR DETERMINATION OF PNEUMOCOCCUS TYPES BY
THE PRECIPITIN REACTION IN THE URINE.

0.5 cc. urine from	Serum Type I. 0.5 cc.	Serum Type II. 0.5 cc.	Serum Type III. 0.5 cc.
Type I case	+	-	-
Type II case	-	+	-
Type III case	-	-	+
Type IV case	-	-	-

"+" indicates precipitin reaction.

This test was tried with urine from cases of pneumonia in children in order to gain familiarity with the test.

A positive reaction varies in intensity from a faint haze to a definite flocculent precipitate and may occur immediately on mixing urine and serum, or after heating for 1 hour at 37°C.

In cases with pneumococcal peritonitis where the result was negative, the urine was concentrated according to the technique of Dochez and Avery (1916). 25 cc. or more of a 24 hour specimen is acidified with a few drops of acetic acid and evaporated down to a volume of about 5 cc. It is then filtered through/

through paper to remove any coagulated albumin, and then 8 to 10 times the volume of 95% alcohol added. The precipitate formed is collected by centrifuging, dried rapidly to remove excess of alcohol and the residue, treated with 2 - 3 cc. of saline which dissolves the specific substance. The clear solution is used as above for the precipitin test.

In all, samples of urine from 4 cases of primary pneumococcal peritonitis were tested.

THE BACTERIOLOGICAL EXAMINATION OF THE CASES.

I have thought it best to give the main clinical details of each case as recorded by the house-surgeon, and after each case to give the results of the bacteriological examination. The reason for this is that the findings vary according to the duration of the disease, and the results of bacteriological examination of an early case are more likely to throw light on the etiology of the disease than the results from a case of a week's duration.

The value of the information lies not in the actual results but of the correlation of the bacteriological findings with the clinical symptoms.

The cases are arranged in chronological order with a short summary of the results of bacteriological examination after each.

CASE No. 1.

J.H. Female child. Age 5 years.

Time between onset of disease and
operation - 10 hours.

Result. Death.

HISTORY. Patient went to her bed last night in her usual good health. About 5 a.m. to-day she complained of abdominal pain, and an hour afterwards she vomited. The pain has been almost continuous since the onset and there have been several attacks of vomiting. Her bowels have been quite regular until to-day, but shortly after the onset of the pain she was given an aperient. There is no frequent or painful micturition.

CONDITION ON ADMISSION. Temperature 102.8°F.

Pulse Rate 144. Respirations 48.

Patient was admitted in the afternoon of the same day she took ill.

The lower portion of the abdomen is fixed and rigid, while the upper portion moves freely on respiration. There is marked tenderness over the lower half of the abdomen, especially on the right side.

No lesions could be found in the chest.

OPERATION./

OPERATION. (10 hours after onset).

The abdomen was opened through the usual appendix grid-iron incision.

The peritoneum of the lower half of the abdomen is covered with a sticky exudate. The pouch of Douglas contains a greenish yellow exudate. The peritoneum of the upper half of the abdomen is glistening. Swabs were taken from the pouch of Douglas and from the upper abdomen.

The patient died at 4.30 a.m. next day, that is, less than 24 hours after the onset of the disease.

RESULTS OF THE BACTERIOLOGICAL EXAMINATION.(1) SWAB FROM THE POUCH OF DOUGLAS.

Films. Abundant capsulated diplococci, with well marked capsules present.

Culture. Pure culture of Pneumococci Type I isolated. Virulence. .01 cc. broth culture fatal for a white mouse in less than 14 hours.

(2) SWAB FROM UPPER PART OF ABDOMEN.

Films. No organisms found.

Culture. No growth.

- (3) BLOOD CULTURE. 2 cc. blood taken.

Pneumococci present in culture
after 36 hours incubation.

- (4) VAGINAL SWAB.

Film. shows coliform organisms and scanty
diplococci.

Culture. (in blood-broth). Abundant coliform
organisms and scanty Gram positive
diplococci present. 1 cc. of this
culture inoculated into a white mouse caused
death in 24 hours. Pneumococci Type I iso-
lated from the heart blood in pure culture.

- (5) THROAT SWAB not taken.

SUMMARY.

- (1) Clinical evidence indicates that the disease
commenced in the lower part of the abdomen.
- (2) Pneumococci present in the exudate in the Pouch
of Douglas. No organisms present in the upper
part of the abdomen, showing that the infection
must have commenced in the pelvis.

(3)/

- (3) Pneumococci are present in the blood stream
10 hours after the onset of the disease.
 - (4) Pneumococci present in the vaginal tract.
 - (5) The pneumococci isolated from the pouch of
Douglas, blood stream and vagina are all of
Type I.
-

CASE No. 2.

A.G. Female child. Age 1 year 10 months.

Time between onset and operation 2 days.

Result. Death.

HISTORY. On September 14th, about 3 p.m. patient felt sick and vomited. At the same time she complained of pain in the right side of the abdomen. The pain and vomiting continued throughout the night.

September 15th. Pain and vomiting still severe.
Patient much worse.

September 16th. Pain was still severe, and the vomiting continued. The bowels were regular on September 14th when the patient was given castor oil and grey powder.

CONDITION ON ADMISSION. (September 17th).

Temperature 105°F. Pulse Rate 168(?).

Respirations 44.

The abdomen is slightly distended. No movement is present on respiration. There is distinct tenderness over the lower half of the abdomen; rather more marked on the right side. There is dullness/

dullness on percussion over the right lower quadrant. Rest of the abdomen is tympanitic.

OPERATION. A grid-iron incision was made over the appendix region.

The peritoneum is oedematous and covered with fibrin. Free pus of a greenish yellow colour is present in the peritoneal cavity. The intestines are covered with purulent fibrin. The appendix is fastened down to the caecum by fibrinous adhesions. The appendix was removed and the abdomen was drained through the wound and suprapubically.

Patient died the following day.

The appendix was sent to the laboratory and sections were examined by the writer, and the following report sent to the Surgeon. "Sections of the appendix show no inflammation of the mucous membrane which is normal. There is recent inflammation of the peritoneal surface with abundant fibrin network and leucocytes."

RESULTS OF BACTERIOLOGICAL EXAMINATION.

(1) PUS FROM THE LOWER ABDOMEN.

Films. Abundant capsulated diplococci present.

Culture. Pure culture of Pneumococcus Type I obtained. Virulence. .01 cc broth/

broth culture kills a white mouse in 24 hours.

(2) PUS FROM THE UPPER ABDOMEN.

A similar result to (1) obtained.

No difference could be found in the severity of the infection in the upper and lower parts of the abdomen.

(3) BLOOD CULTURE. 2 cc. blood taken.

Pneumococci, Type I present in culture after 48 hours incubation.

(4) VAGINAL SWAB.

Film. Scanty diplococci present.

Culture. Scanty colonies of pneumococci present on blood agar, and contaminated with B. Coli and B. Subtilis. Culture inoculated into a white mouse which was found dead in 36 hours. Pneumococci Type I isolated from the heart blood.

(5) THROAT SWAB.

Film. Gram positive diplococci present.

Culture. Colonies of Pneumococci picked off. Organism is Type I.

- (6) URINE. No cystitis present. Precipitin test was not done.

SUMMARY.

- (1) As far as could be ascertained by films and cultures, the infection in the upper and lower abdomen was equally severe. (Duration of disease, 2 days).
- (2) Pneumococci were present in the blood stream.
- (3) Pneumococci were present in the vagina.
- (4) Pneumococci were present in the throat.
- (5) Pneumococci from the above sources were all of the same Type. (Type I.).

CASE No. 3.

E.F. Female child, age $4\frac{1}{2}$ years.

Onset of disease noon 3.10.20.

Operation - night 6.10.20.

Time between onset and operation -
3 days 10 hours.

Result. Death. 10.10.20.

HISTORY. The child was in her usual health until mid-day on Sunday, October 3rd, when she suddenly complained of abdominal pain.

Shortly after this she vomited. The same day she complained of pain on micturition. The abdominal pain was constant in character and at times made her cry out. She did not sleep on Sunday night, and on Monday was no better. She vomited a little on Monday morning and her condition remained more or less the same until her admission on Wednesday. No history of diarrhoea was recorded.

CONDITION ON ADMISSION. Temperature 102.6°F .

Pulse 144. Respirations 56.

The child is flushed and looks ill.

The abdomen is "full" and rigid. There is marked tenderness over the lower half. There is dullness on/

on percussion in both flanks.

There is nothing abnormal to be found in the chest.

The urine shows nothing abnormal.

OPERATION. On opening the abdomen, the peritoneal cavity is found full of greenish yellow pus containing flakes of fibrin. The infection seems equally severe over all the abdomen.

RESULTS OF BACTERIOLOGICAL EXAMINATION.

(1) PUS FROM LOWER ABDOMEN.

Films. Show very abundant capsulated diplococci.

Cultures. Pure culture of pneumococci Type I isolated. Virulence - .01 cc. broth culture kills a white mouse in 24 hours.

(2) PUS FROM UPPER ABDOMEN.

Films. Show very abundant capsulated diplococci.

Cultures. Pure culture of pneumococci Type I isolated.

(3) BLOOD CULTURE. 1.5 cc. blood taken.

Abundant growth of pneumococci, Type I, obtained in 24 hours.

(4) VAGINAL SWAB.

Films. Scanty diplococci present in a mixed infection.

Culture. (in blood broth). Mixed culture containing Gram-positive diplococci.
 * Culture was fatal for a mouse in 36 hours. Heart blood gave a pure culture of pneumococci, Type I.

(5) THROAT SWAB.

Films show a mixture of organisms; some Gram-positive diplococci being present.

Culture. Mixed culture containing diplococci obtained. Culture injected into a white mouse. The mouse remained healthy after 4 days.

(6) URINE. No cystitis present. Precipitin test not done.

SUMMARY.

(1) No difference in the severity of the infection of the upper and lower abdomen could be found. Pneumococcus Type I present.

(2) Pneumococci present in the blood stream.

(3)/

- (3) Pneumococci isolated from the vaginal discharge.
 - (4) The pneumococci from the above sources were all of the same Type.
 - (5) No virulent pneumococci present in the throat.
-

CASE No. 4.

C.D. A female child, age 6 years 2 months.

Onset of the disease morning 15.12.20.

Operation - 5 p.m. 16.12.20.

Time between onset and operation 30 hours.

Result. Death. 24.12.20.

HISTORY. A month prior to admission patient was ill for a week complaining of an attack of vomiting followed by pain and tenderness in the right side. Poultices were applied and the symptoms rapidly disappeared. (This was probably an infection of the Fallopian tube).

PRESENT ILLNESS. The onset was sudden on the morning of December 15th while the child was at school. There was a sharp attack of pain which "doubled the child up", and which was accompanied by vomiting. The pain remained constantly in the right side and the vomiting continued. There was no diarrhoea. In the evening she complained of hot, painful micturition, and the frequency was 4 or 5 times per hour. This frequency lasted for about 14 hours.

CONDITION ON ADMISSION. The child is very irritable and shouts with pain on being touched.

The lower half of the abdomen does not move with respiration. Nothing abnormal can be found in the chest. There is no record in the case history of vaginitis. The breath smells strongly of acetone. Temperature is subnormal - 97°F. Pulse rate 132. Respiration rate 30. Urine contains no albumen, pus, or casts.

OPERATION. at 5 p.m. 16.12.20. (30 hours after onset of symptoms.)

On opening the abdomen, the intestines are seen to be covered with a sticky exudate. The pelvis contains free fluid and flaky pus. The child died 24.12.20. No post-mortem examination allowed.

RESULTS OF BACTERIOLOGICAL EXAMINATION.

(1) PUS FROM LOWER ABDOMEN.

Films show very abundant capsulated diplococci.

Cultures. Abundant growth of pneumococcus Type I obtained. Virulence, .001 cc. broth culture fatal for a white mouse in 24 hours.

(2) SWAB FROM UPPER ABDOMEN.

Films. Show capsulated diplococci but organisms are rather scanty.

Cultures. Scanty growth of pneumococci in serum broth and on serum agar. Organism belongs to Type I.

(3) BLOOD CULTURE. 1 cc. of blood taken.

Abundant growth of pneumococci Type I obtained after 24 hours incubation.

(4) VAGINAL SWAB.

Films Show a mixture of organisms. Gram-positive diplococci are present.

Culture. Mixed culture obtained. Gram-positive cocci present but are much overgrown. Culture injected into a white mouse which died within 36 hours. Pure culture of pneumococcus Type I, isolated from the heart blood.

(5) THROAT SWAB.

Film. Showed a mixture of organisms, with fairly numerous Gram-positive diplococci.

Culture./

Culture on serum agar plate. Pneumococci easily isolated. The organism belongs to Type IV. Pure culture inoculated into a mouse. The mouse survived.

(6) URINE. Precipitin test was not done.

SUMMARY.

- (1) Heavier infection with the pneumococcus of the lower abdomen than of the upper.
 - (2) Pneumococci present in the blood stream 30 hours after the onset of the disease.
 - (3) Virulent pneumococci isolated from the vagina.
 - (4) The pneumococci from the above three sources are all of the same Type, namely, Type I.
 - (5) Pneumococci isolated from the throat are of a different Type, namely, Type IV.
-

CASE No.5.

M.McD. A female child, age 6 years 9 months.

Onset of the disease 11 p.m. 26.12.20.

Operation - 7.30 p.m. 27.12.20.

Time between onset and operation 21 hours.

Result. Died. 7.1.21.

HISTORY. Patient was quite well up to 11 p.m. on December 26th when she suddenly complained of pain in the "middle of the stomach".

Soon afterwards she began to vomit and she vomited several times during the night. She did not cry with pain but moaned in her sleep. Her bowels became somewhat loose. There was no frequent or painful micturition.

CONDITION ON ADMISSION. Temperature 102.6°F.

Pulse rate 160. Respiration rate 40.

The lower half of the abdomen, which is slightly distended does not move freely on respiration. The abdomen is tender all over and particularly in the right lower quadrant. Both recti are rigid, particularly the right.

OPERATION./

OPERATION. (21 hours after the onset of symptoms.)

The pouch of Douglas contains a small amount of pus of thin consistence which has no odour.

The intestines are not very congested and are not sticky.

The appendix is apparently normal.

The pelvis was drained suprapubically, and the right iliac fossa was drained from the operation wound.

RESULTS OF BACTERIOLOGICAL EXAMINATION.

(1) SWAB FROM THE LOWER ABDOMEN.

Films. Fairly abundant capsulated diplococci present.

Culture. Pure culture of pneumococci Type I isolated. Virulence; .01 cc. broth culture kills a white mouse in 24 hours.

(2) SWAB FROM THE UPPER ABDOMEN.

Films. Capsulated organisms present, but the proportion of organisms to cells seems less than in (1).

Culture./

Culture. Growth on solid media are less profuse than in (1). Type I pneumococcus present.

(3) BLOOD CULTURE. 2 cc. of blood taken.

Abundant culture of pneumococcus Type I present after 16 hours incubation.

(4) VAGINAL SWAB.

Films. Show mixed infection with Gram-positive diplococci present.

Culture. Rabbit blood broth culture was overgrown with other organisms particularly B. Coli.

Diplococci were found in films. Mouse was inoculated with culture and was found dead after 36 hours. Pure culture of pneumococci Type I was isolated from the heart blood.

(5) THROAT SWAB.

Films. Show a mixture of organisms to be present including Gram-positive diplococci.

Cultures. Plate culture shows pneumococci to be present. Culture was inoculated into a white mouse which died in 36 hours. Pneumococcus Type I obtained from the heart blood.

- (6) URINE. Nothing abnormal found. Precipitin reaction not done.

SUMMARY.

- (1) Infection of the lower abdomen seems more severe than in the upper abdomen.
- (2) Pneumococci present in the blood stream 21 hours after the onset of the disease.
- (3) Virulent pneumococci are present in the vagina.
- (4) Virulent pneumococci are present in the throat.
- (5) All the pneumococci isolated from the above sources are all of Type I.

CASE No. 6.

J.I. A female child, age 4 years.

Time between onset of disease and
operation - 2 days.

HISTORY. Patient was perfectly well up to the morning of December 1st. She then complained of pains across the lower part of the abdomen - below the umbilicus. At 10 a.m. she received a dose of castor oil, and her bowels moved 6 times that day. Previously the child was inclined to be constipated. The child was kept in bed and about 7 p.m. she vomited.

On December 2nd she still complained of pain in the lower part of the abdomen and in the left Subcostal area. There was no vomiting. A doctor was called in and he saw the child about 1 p.m. The temperature was then 103°F. The doctor auscultated the chest and palpated the abdomen. He informed the mother that the chest was free of trouble, and having elicited tenderness in the right iliac region he sent her to the Hospital as a case of "acute appendicitis". There was no history of frequency of micturition.

CONDITION/

CONDITION ON ADMISSION. (4.30 p.m. December 2nd)

Temperature 99°F. Pulse rate 132.

Respiration rate 44. The patient does not look toxaemic although the face is flushed.

Chest. Percussion shows equal and normal resonance to be present. On auscultation there is vesicular breathing only and no evidence of any infection.

Abdomen moves fairly freely. There is slight tenderness present on the left side at the level of the umbilicus. There is no pain or tenderness over the appendix region.

The case was placed under observation.

On December 3rd, a slight central distension was noticed in the region of the umbilicus. The abdominal wall is not moving so freely, especially the lower half. On palpation there is now tenderness in the right iliac fossa over the brim of the pelvis. Per rectum, slight "fullness" and apparently tenderness present. Rigidity is definitely present in the abdominal muscles.

Respirations 33 per minute and normal in character.

The lungs are quite clear and the breathing is vesicular.

Heart sounds are normal.

OPERATION./

OPERATION. (2 days after onset of symptoms).

A small incision was made in the middle line of the abdomen below the umbilicus.

On opening the peritoneum, the intestines are seen to be sticky and there is a small amount of purulent fluid in the pouch of Douglas. The appendix is normal. The abdomen was then closed and drained.

On December 25th the patient's temperature rose to 102°F.

December 29th An empyema was suspected, the chest was explored and 80 cc. of pus removed.

December 30th A rib was resected.

January 2nd. Patient was removed from the hospital at the request of the parents.

She was improving but was not cured.

RESULTS OF BACTERIOLOGICAL EXAMINATION.

(1) PUS FROM LOWER ABDOMEN.

Films showed abundant capsulated diplococci.

Culture. Pure culture of Type II isolated.

(2) SWAB FROM UPPER ABDOMEN.

Films. Capsulated diplococci present but not abundant.

Cultures. A more scanty growth of Type II pneumococcus than in (1) obtained. Virulence .01 cc. broth culture is fatal for a white mouse in 48 hours.

- (3) BLOOD CULTURE. 3 cc. of blood taken. Pneumococcus Type II present after 24 hours incubation.

(4) VAGINAL SWAB.

Films. Show scanty Gram-positive diplococci to be present.

Culture. Mixed culture of B.Coli and diplococci. Mouse injected with the culture was found dead in 36 hours. Type II Pneumococcus isolated.

(5) THROAT SWAB.

Film. Abundant Gram-positive diplococci present.

Cultures. Mixed culture obtained but colonies of pneumococci could be picked off. Organism belongs to Type II.

(6)/

- (6) FLUID FROM EMPYEMA. Type II pneumococci were easily isolated.

SUMMARY.

- (1) This is a case of primary pneumococcal peritonitis due to a Type II organism of low virulence.
 - (2) There is evidence that the pelvis is more heavily infected than the upper part of the abdomen.
 - (3) Pneumococci present in the blood stream.
 - (4) Virulent pneumococci isolated from the vagina.
 - (5) Pneumococci present in the throat.
 - (6) All the pneumococci from the above sources belonged to Type II.
 - (7) An empyema followed 3 weeks after the onset of the disease and was due to Type II pneumococci.
-

CASE No. 7.

R.G. A female child, age 4 years.

Onset of the disease 7 a.m. 2.6.21.

Operation evening 2.6.21.

Time between onset and operation 12 hours.

Result. Death. 17.6.21.

HISTORY. The child was perfectly well on June 1st and slept well all that night. At 7 a.m. on June 2nd she complained of abdominal pain. The onset of the pain was not described as being sudden, but it came on somewhat gradually. About 9 a.m. she began to vomit. Since then she has lain quiet, has suffered considerable pain, has had great thirst, and frequently vomited the water she was given to drink.

CONDITION ON ADMISSION. (afternoon, June 2nd).

Temperature 101°F. Pulse rate 180.

Respiration rate 36.

Abdomen. Respiratory movements are much restricted. The abdomen is not distended. Light touch and percussion cause pain all over the abdomen, but more particularly round the umbilicus. Muscular resistance is not so constant a feature as is usual in peritonitis./

peritonitis. There is pain, tenderness and rigidity over all the abdomen.

Chest. No physical signs, either of bronchitis or of pneumonia present.

There is a slight but distinct redness of the vulva and a slight sticky discharge.

No history of frequency of micturition was recorded in the notes.

OPERATION. (June 2nd).

There is a sticky purulent exudate in the abdomen, especially marked in the pelvis.

RESULTS OF BACTERIOLOGICAL EXAMINATION.

(1) SWAB FROM THE LOWER ABDOMEN.

The swab is covered with abundant greenish-yellow pus.

Films. Very abundant capsulated diplococci present.

Culture. Pure culture of pneumococci, Type I, obtained. Virulence, .01cc. broth culture kills a white mouse in 16 hours.

(2)/

(2) SWAB FROM THE UPPER ABDOMEN.

The swab is covered with dryish, fibrinous material.

Films. Capsulated diplococci present but relatively scanty compared with films from (1).

Culture. Pure culture of pneumococci, Type I, obtained.

(3) BLOOD CULTURE. 2 cc. of blood taken.

Abundant growth of pneumococci obtained after 16 hours incubation. Type I organism present.

(4) VAGINAL SWAB.

Films show abundant coliform organisms, diphtheroid bacilli, and scanty Gram-positive diplococci.

Culture. Colonies of pneumococcus Type I isolated direct from blood-agar plates. Virulence, .1 cc. broth culture kills a mouse within 24 hours.

(5) THROAT SWAB.

Film. Mixed infection of organisms with Gram-positive diplococci present.

Culture./

Culture. Profuse, with both streptococci, pneumococci and M. Catarrhalis present in film.

Mouse injected with culture and was found dead 38 hours afterwards.

Pneumococcus Type I obtained from the heart blood.

(6) URINE.

Precipitin reaction done but was negative.

SUMMARY.

- (1) At operation, the pelvis is seen to be more heavily infected than the upper part of the abdomen. This difference in degree of infection is well seen on comparing the exudates from these regions.
- (2) Organisms are present in the blood stream 12 hours after the onset of the disease.
- (3) Virulent pneumococci are present in the vaginal secretion.
- (4) Virulent pneumococci are present in the throat.
- (5) The pneumococci isolated from the above sources are all of Type I.
- (6) Precipitin reaction in the urine is negative.

CASE No. 8.

E.P. A female child, age 3 years 3 months.

Onset of the disease 9 a.m. 7.6.21.

Operation - evening 10.6.21.

Time between onset and operation $3\frac{1}{2}$ days.

Result. Death. 11.6.21.

HISTORY. On June 7th at 9 a.m. patient complained of pain in the lower abdomen on rising.

The pain became less severe during the day, but was worse at night. She vomited during the evening.

On June 8th she continued to complain of pain in the lower abdomen at intervals. She vomited twice that day, slept very badly during the night and complained of thirst.

On June 9th the pain was still severe and the vomiting continued. A swelling of the lower abdomen was now noticed. The bowels were inclined to be constipated.

No urinary symptoms were noted in the case history.

CONDITION ON ADMISSION. June 10th.

Temperature 101°F. Pulse rate 163.

Respiration rate 36.

The abdomen shows no respiratory movement.

The lower half is considerably distended and rigid.

No lesions can be found in the chest.

The vulva and vagina are distinctly inflamed.

OPERATION. On opening the abdomen a generalised peritonitis is seen to be present.

The pus is greenish-yellow in colour and contains flakes of fibrin.

RESULTS OF BACTERIOLOGICAL EXAMINATION.

(1) PUS FROM THE LOWER ABDOMEN.

Films show abundant capsulated diplococci to be present.

Cultures. Pure culture of pneumococcus Type I obtained. Virulence, .01 cc. broth culture kills a white mouse in 16 hours.

(2) PUS FROM THE UPPER ABDOMEN.

A similar result to (1) was obtained.

(3) BLOOD CULTURE. 2 cc. of blood taken.

Abundant pneumococci present after 24 hours incubation. Organism belongs to Type I.

(4) VAGINAL SWAB.

Films. Show a mixed infection; numerous Gram-positive diplococci are present.

Culture on blood agar. Pneumococci isolated direct from plate culture. Organisms belong to Type I.

(5) THROAT SWAB.

Films show a mixed infection with some Gram-positive cocci present.

Culture. Hopelessly overgrown with B. Subtilis.

(6) URINE. Precipitin reaction is positive, Type I.

SUMMARY.

- (1) There is a heavy infection with the pneumococcus throughout the abdominal cavity. No difference could be found between the severity of the infection in the upper and lower abdomen. Disease was of $3\frac{1}{2}$ days duration.
- (2) Pneumococci present in the blood stream.
- (3) Abundant pneumococci present in the vulvitis and vaginitis discharge.
- (4) All the pneumococci from the above sources were of Type I.
- (5) No results were obtained from the throat swab.
- (6) Precipitin reaction was positive, Type I.

CASE No. 9.

F.Y. A female child, age 6 years 5 months.

Onset of disease 21.9.21.

Operation - 27.9.21.

Interval between onset and operation -
6 days.

Result. Recovery.

HISTORY. On September 21st, patient had a sudden
attack of abdominal pain while at school.

The pain was most severe round the umbilicus.

No vomiting occurred. She was feverish and restless
all night.

On September 22nd, the pain continued severe. The
child had no appetite and was thirsty and feverish.
Diarrhoea commenced and the stools contained mucus.
The patient remained in this condition until September
24th, when she complained of pain on micturition.

CONDITION ON ADMISSION. (September 27th).

Temperature 101.8°F. Pulse rate 136.

Respiration rate 36.

Abdomen. Rigidity is present over the
whole of the abdomen and is most marked
on the right side. No movement is seen on respiration.
There is tenderness present on palpation and on light/

light percussion. The tenderness is most marked in the lower half of the abdomen. On rectal examination there is tenderness present and the pouch of Douglas is felt to contain fluid exudate.

No lesions could be found in the chest.

OPERATION. September 27th (6 days after onset of disease)
Grid-iron incision made on the right side.

The lower abdomen is full of greenish-yellow "pneumococcal" pus. Appendix inspected but no primary inflammatory condition is present.

The abdomen was then partially closed and drained.

SUBSEQUENT HISTORY.

September 28th. Cough commenced.

September 30th. Consolidation present, affecting one lobe in each lung.

October 2st. Transfusion done with 320 cc. of blood.

Later the chest condition became better.

Towards the end of October a "low" faecal fistula formed.

January 13th. Fistula still discharging, child sent to a convalescent home.

RESULT/

RESULT OF BACTERIOLOGICAL EXAMINATION.

(1) & (2).

The pus from both the upper and lower parts of the abdomen gave similar results.

Films. Abundant capsulated diplococci present.

Culture. Pure culture of pneumococcus Type I obtained. Virulence, .01 cc. broth culture fatal for a white mouse in 30 hours.

(3) BLOOD CULTURE. (2.5 cc. in 100 cc. broth).

Pneumococci Type I present after 3 days incubation.

(4) VAGINAL SWAB.

Films. Very scanty diplococci present; mixed infection.

Culture. Scanty diplococci, culture was much overgrown by other organisms.

Mouse inoculated - found dead in 36 hours. Pneumococcus Type I isolated from the heart blood in pure culture.

(5) THROAT SWAB.

Films. Abundant Streptococci and M. Catarrhalis, but scanty diplococci present.

Culture. Profuse growth, no pneumococci colonies seen, but Gram-positive diplococci are seen in film.

Mouse inoculated found dead in 36 hours.

Pneumococcus Type I isolated from heart blood.

(6) URINE. Precipitin test was negative.

SUMMARY.

- (1) Abundant pneumococcal pus present 6 days after onset. Pneumococci Type I isolated.
- (2) No difference can be found in the severity of the infection in the upper and lower abdomen.
- (3) Pneumococci were present in the blood stream even at this stage of the disease, but very scanty in number.
- (4) Pneumococci were isolated from vagina.
- (5) Pneumococci were isolated from throat.
- (6) All these pneumococci were of the same Type, (Type I).
- (7) This is an example of chronic pneumococcal peritonitis, with fistula formation, and recovery.
- (8) Diarrhoea and pain on micturition present indicative of pelvic irritation.

CASE No. 10.

C.L. A female child, age 4 years.

Onset of the disease, evening 11.1.22.

Operation - evening 13.1.22.

Time between onset and operation, about
48 hours.

Result. Died 21.1.21.

HISTORY. The child suddenly became ill on the evening of January 11th, when she felt a sudden and severe pain in the lower part of the abdomen. Vomiting began soon after the pain. She was given an aperient, but she immediately vomited it.

January 12th. She continued to have pain which came on in spasms, and the vomiting occurred from time to time. Diarrhoea now commenced and the child became very thirsty.

There was no frequent or painful micturition.

CONDITION ON ADMISSION. January 13th.

Temperature 102.2°F.

Pulse rate 140.

Respiration rate 60. The child is very drowsy and toxic looking. The tongue is very dirty and the patient/

patient complains of thirst. The abdomen seems distended, and there is slight movement on respiration. There is rigidity and tenderness all over the abdomen. No lesion to be found in the chest.

OPERATION. Abdomen was opened and the appendix appeared to be normal. A generalised peritonitis was seen to be present and there was pus in the pouch of Douglas.

RESULTS OF BACTERIOLOGICAL EXAMINATION.

(1) SWAB FROM LOWER ABDOMEN.

Films. Shows numerous capsulated diplococci.

Culture. Pure culture of Pneumococcus Type II obtained. Virulence, .01 cc. inoculated into a white mouse at 5 p.m. Mouse found stiff next morning. Films from heart blood showed an intense septicaemia.

(2) SWAB FROM UPPER ABDOMEN.

Result similar to above.

(3) BLOOD CULTURE. Abundant pneumococci, Type II, present after 48 hours inoculation.

(4)/

(4) VAGINAL SWAB.

Films. Organisms are scanty, but both Coliform organisms and Gram-positive diplococci were present.

Culture. On serum agar. Very scanty cocci were present. The whole culture was emulsified in 1 cc. of saline and injected into a white mouse. The mouse was found dead in 36 hours, and Pneumococci Type II were isolated from the heart blood.

(5) THROAT SWAB. was not taken.

(6) URINE. Precipitin test gave a faint positive.

SUMMARY.

- (1) There is no appreciable difference in the severity of the infection in the upper and lower abdomen. The organism is very virulent.
- (2) Pneumococci were present in the blood stream.
- (3) Virulent pneumococci were present in the vagina.
- (4) Pneumococci from the above sources were all of Type II. This type is uncommon in children.
- (5) Precipitin test was faintly positive.

TABLE SUMMARISING THE RESULTS OF BACTERIOLOGICAL EXAMINATION OF THE CASES.

Case No.	Name	Age in years.	Sex.	Duration before operation.	Time between onset & death.	Lower Abdomen	Upper Abdomen	Blood Culture	Vagina	Throat	Urine	Result	Post Mortem
1.	J.A.	5	F	10 hours	23½ hrs.	++(1)	-	+(1)	+(1)	0	0	Fatal	0
2.	A.G.	10 $\frac{10}{12}$	F	2 days	3 days	++(1)	++(1)	+(1)	+(1)	+(1)	0	Fatal	0
3.	E.F.	4½	F	3 days 10 hrs.	8½ days	++(1)	++(1)	+(1)	+(1)	0	0	Fatal	+
4.	C.D.	6 $\frac{2}{12}$	F	30 hours	9 days	++(1)	+(1)	+(1)	+(1)	+(IV)	0	Fatal	0
5.	M.McD.	6 $\frac{1}{12}$	F	21 hours	8 days	++(1)	+(1)	+(1)	+(1)	+(1)	0	Fatal	+
6.	J.I.	4	F	2 days	-	++(II)	+(II)	+(II)	+(II)	+(II)	0	Recov- ery.	0
7.	R.G.	4	F	12 hours	25 days	++(1)	+(1)	+(1)	+(1)	+(1)	-	Fatal	0
8.	E.F.	3 $\frac{3}{12}$	F	3½ days	7½ days	++(1)	++(1)	+(1)	+(1)	-	+(1)	Fatal	+
9.	F.Y.	6 $\frac{5}{12}$	F	6 days	-	++(1)	++(1)	+(1)	+(1)	+(1)	-	Recov- ery.	0
10.	C.L.	4	F	2 days	10 days	++(11)	++(II)	+(II)	+(II)	0	+(II)	Fatal	0

0 means specimen not obtained. + means positive and number following in brackets represents the Type of pneumococcus. - means specimen examined but negative.

OBSERVATIONS ON THE PERITONEAL EXUDATE.

FILM PREPARATIONS.

(1) Organisms present. Film preparations showed very abundant pneumococci in the pus. This great proportion of organisms to pus cells is noticeable pneumococcal infections, such as meningitis, pneumonia, and abscess formation. The organisms were of the typical "flame" or "lanceolate" shape, and the capsule was exceedingly well marked. In no other pneumococcal exudate have I found such well marked capsulation as in primary pneumococcal peritonitis.

(2) Cells. The majority of the cells consist of polymorphonuclear leucocytes. There are also present large mononuclear cells derived from the peritoneal endothelium. Phagocytosis is often well marked.

In the earliest stages of the disease there is a much heavier infection with pneumococci in the pelvis than in the upper abdomen. This has been demonstrated in early cases of the disease by inspection/

inspection at operation. This difference in severity can also be shown by examining smears and also by plating out the exudate from different parts of the abdominal cavity. In smears the proportion of cocci to pus cells is much greater in the pelvic pus than in the upper abdominal exudate.

In one very early case, where the only lesion noticed at the operation was a film of fibrin over the uterine appendages, pneumococci could not be demonstrated, either by microscopic examination or on culture, in the upper part of the peritoneal cavity, whereas they were easily isolated from swabs from the pelvis.

OBSERVATIONS ON THE BLOOD CULTURES.

All blood cultures were positive, and pneumococci could be demonstrated usually after 24 hours incubation, although on one occasion it was not until after 72 hours in the incubator that organisms could be detected microscopically. The number of pneumococci present per cubic centimetre in the blood, could not be definitely ascertained as the majority of operations were "emergencies" and at a time inconvenient for melting and plating out agar.

From the very profuse growth of organisms usually obtained/

obtained after 24 hours incubation, it is probable that the circulating blood must have been well infected with the pneumococcus..

It has been my experience that pneumococci gain access to the blood stream more frequently and in greater numbers in children than in adults. The Rockefeller Institute workers in their Monograph On Pneumonia (1917), consider 15 or more pneumococci per cubic centimetre of blood, a very bad prognostic sign. Their observations were made on adults, but I do not think these results hold good for children. The exact significance of the presence of organisms in the blood stream is not fully understood, as some children, especially in pneumonia, may survive a bacteriaemia with more than 50 organisms per cubic centimetre in the blood. At the same time it must be admitted that of the 9 cases here described in which there was a heavy pneumococcal infection of the blood, 8 were fatal. The whole subject of organisms in the blood stream needs serious investigation.

OBSERVATIONS ON THE VAGINAL FLORA.

Throat swabs were taken in all of the 10 cases examined. In every case pneumococci were isolated, but often only with difficulty owing to the relatively/

relatively small number of pneumococci present, and contamination with other organisms. This difficulty is emphasised because ordinary plating methods are not sufficient, and anyone repeating these experiments would fail to isolate pneumococci from the vaginal flora in many cases, unless the difficulties of so doing were appreciated. Most of the organisms were isolated only by injecting young white mice with comparatively large quantities of rabbit-blood broth or serum broth cultures.

In all cases the Type of pneumococcus isolated was of the same type as the organism isolated from the peritoneal cavity and from the blood stream.

OBSERVATIONS ON THE PRESENCE OF PNEUMOCOCCI IN THE THROAT.

Throat swabs were taken from 7 of the 10 cases of pneumococcal peritonitis examined bacteriologically. The pneumococcus was isolated in 6 of these 7 cases. In 5 cases the Type of pneumococcus was the same as that causing the peritonitis. In one case, a Type I pneumococcus was isolated from the abdomen, blood stream and vagina, whereas the pneumococcus isolated from the throat belonged to Type IV.

In/

In one case, organisms resembling pneumococci were present in the culture, but on inoculation of a mouse to isolate the organism, the animal did not die and the organism was not recovered.

OBSERVATIONS ON THE EXAMINATION OF THE URINE.

The urine was not systematically examined in the present series of cases.

When examined, the urine showed no evidence of cystitis. The chlorides present were reduced, but owing to the ages of the children and the state of collapse after operation, it was not possible to obtain a 24 hours specimen of urine for determining the degree of reduction of the chlorides.

The precipitin test was done in 4 cases. Of these, 2 were completely negative, one was positive with unconcentrated urine, whilst in one case there was a faint positive after concentrating the urine.

SUMMARY OF THE RESULTS OF BACTERIOLOGICAL EXAMINATION
OF 10 CASES OF PRIMARY PNEUMOCOCCAL PERITONITIS.

- (1) In every case the causal organism was proved to be the pneumococcus.
- (2) In 8 cases the organism belonged to Type I, and in the remaining 2 cases, a Type II pneumococcus was isolated. In no case was infection due to organisms of Type III or Type IV.
- (3) Pneumococci were isolated from the peritoneal cavity, blood stream and vagina in every case examined. The organisms obtained from these three sources were all of the same type in each individual.
- (4) In one case, the pneumococcus from the throat was a different type from the organisms isolated from the abdomen, blood stream and vagina.
- (5) In early cases, there is a heavier infection in the lower abdomen than in the upper abdomen.
- (6) In one case, pneumococci could not be demonstrated in the upper abdomen, whereas they were easily isolated from the pelvis.

These results are entirely in support of the view that the infection reaches the peritoneum by way of the genital tract.

The inflammation in the early cases is most severe in the lower abdomen, and in one case the infection was confined entirely to the pelvis, thus showing that the disease commences in the pelvis.

Pneumococci can be demonstrated in the vagina in all cases and are of the same Type as the organisms in the peritoneal cavity. Here then we have a peritonitis with an open path of infection from the outside, and pneumococci of the same Type at both ends of this path. It is not unreasonable to conclude that the route of infection of the peritoneum was along this path.

As pneumococci were found in the vagina 10 hours after the onset of the disease, it is very unlikely that these organisms made their way downwards from the peritoneum in that time.

The observation that in one case, a different Type of pneumococcus from the one causing infection of the peritoneum, was isolated from the throat, is most significant. The infecting pneumococcus was not present in the throat hence the organism could not have/

have gained access to the body from the tonsils. Neither could the infecting organism have been swallowed with the sputum, and so gained entrance to the peritoneal cavity from the intestinal canal. No other lesions were present in this case and the infection was not from the mouth or alimentary tract. Virulent pneumococci of the same Type as that causing the infection were present in the vagina, and as the other possible modes of infection are shown to be impossible we conclude therefore that the infection must have reached the peritoneal cavity from the vagina by way of the uterus and Fallopian tubes.

RESULTS OF THE POST-MORTEM EXAMINATIONS.

It is to be regretted that permission for autopsy was obtained only in 3 of the 8 fatal cases.

A thorough examination of the patient during life loses much of its value if the information so obtained is not verified after death.

In this series of cases I was unable to investigate the fulminating type of the disease, as the 3 cases examined died 7, 8 and $8\frac{1}{2}$ days respectively after the onset of the disease.

As the fatal termination in pneumococcal peritonitis is usually due to a septicaemia, no reliance can be placed on the presence of pneumococci in any organ or any secretion when examined post-mortem. Moreover the time elapsing between death and the autopsy permits a multiplication of the organisms, and no conclusions of any value can be drawn from the results of such an investigation.

As this investigation is concerned primarily with the etiology of the disease, only evidence bearing directly on the route of infection is given.

It is obvious that after the disease has been in progress for a week, it is difficult to determine exactly/

exactly where the infection commenced, as the inflammation is diffused throughout the abdominal cavity and is equally severe in every part.

The important points for investigation are:-

- (1) Presence of any other pneumococcal focus of infection, such as in the lungs.
- (2) Any evidence supporting the intestinal theory of infection.
- (3) Any evidence in support of the view that infection is by the genital tract.

In the three cases examined, the peritoneal cavity was the only focus of inflammation. The lungs were healthy on macroscopic and microscopic examination. The tonsils showed nothing abnormal. The middle ear was carefully examined in each case and was never found diseased.

The intestines were examined very carefully. The peritoneal surface was coated with greenish-yellow purulent fibrin and the bloodvessels were dilated. No lesion of the intestinal mucous membrane could be found and the Peyer's patches appeared healthy and were not increased in size. Microscopic examination of the Peyer's patches revealed no evidence/

evidence of any inflammation. The intestinal canal was carefully examined from stomach to rectum and no evidence in favour of infection through the bowel wall could be obtained.

The mesenteric glands were not unduly enlarged as would be expected if the infection came through the intestinal wall.

The genital tract was carefully examined in each of the three cases.

The Fallopian tubes were covered with a layer of purulent fibrin, and on removing this exudate the tubes were seen to be congested. On opening the tubes no evidence of salpingitis was found. Cultures made from the lumen of the Fallopian tubes showed the presence of pneumococci.. This observation however has no significance as the patients died of septicaemia, and pneumococci could be found in the pleural cavity and on the membranes of the brain. The body of the uterus appeared normal.

Microscopical examination of the Fallopian Tubes.

On section the mucous membrane is healthy and shows little or no desquamation of epithelial cells. The bloodvessels under the peritoneum are dilated, and inflammatory exudate is seen on the peritoneal surface. In sections stained by Gram's method, pneumococci/

pneumococci may be seen in the lumen of the tube and abundant pneumococci are to be found in the exudate on the peritoneal coat.

On microscopic examination, the mucous membrane of the uterus shows no evidence of inflammation, and the vaginal wall appears normal.

The other organs of the body show the usual toxic changes consequent upon an acute infection.

The appearance of the Fallopian tubes is very interesting. The absence of inflammation of the mucous membrane indicates that if the infection came by way of the genital tract it was not by direct extension along the tubes. It would appear that the organism does not exert any pathogenic effect whilst in the Fallopian tube, but only on its emergence into the peritoneal cavity does it give rise to inflammation. From a consideration of the clinical histories it is seen that there are no symptoms suggestive of tubal inflammation before the onset of the abdominal pain. The peritonitis is therefore the first indication of the presence of the pneumococcal infection.

We have a similar parallel in the case of acute lobar pneumonia which also commences in healthy individuals as a "bolt from the blue". Post-mortem examination/

examination of a rapidly fatal case of lobar pneumonia usually shows no evidence of inflammation of the trachea or bronchi, and the only pneumococcal lesion found is the pulmonary one.

These two diseases, lobar pneumonia and primary pneumococcal peritonitis, are similar inasmuch that the organism may cause inflammation of the tissues without exerting any pathogenic effect along the paths of infection.

SUMMARY.

- (1) The peritonitis was the only pneumococcal lesion present.
- (2) No focus of infection could be found in the lungs or middle ear.
- (3) There is no evidence of any infection from the intestinal canal.
- (4) The genital tract shows no evidence of direct spread by inflammation, of the infection along the uterus and Fallopian tubes.
- (5)/

- (5) The pneumococcus passes along the genital tract without causing any inflammation or symptoms, and it is only when the organisms reach the peritoneal cavity that they become pathogenic.
 - (6) The sudden onset of the disease in a healthy individual is entirely in accordance with this view of infection.
-

OBSERVATIONS ON THE VAGINAL FLORA IN CHILDREN.

The bacteriological examination of cases of primary pneumococcal peritonitis has shown that the pneumococcus is present in the vaginal secretion in all cases of the disease.

The question therefore naturally arises as to whether the pneumococcus is present in the vaginal secretion of normal children, and if so, under what conditions.

At the Royal Hospital for Sick Children, Edinburgh, I have frequently to examine smears of vaginal secretion for the presence of gonococci. Before the present work was commenced I had noticed that Gram-positive diplococci, suggestive of pneumococci were to be found in these smear preparations.

It was also noticed that these organisms were found in material from the Out-patient Department and were not present in the few smears sent in from the Wards.

An examination was therefore made of the secretion obtained from the entrance of the vagina in children, to determine the presence of the pneumococcus. The technique employed was the same as for the vaginal swab from cases of pneumococcal peritonitis.

The following is the summary of the results obtained.-

- (1) In children of the lower classes there are usually signs of vaginal irritation (pus cells) and a mixed flora of organisms.
- (2) Pneumococci can frequently be isolated from the secretion by direct plating on rabbit-blood agar.
- (3) These pneumococci are usually non-pathogenic and belong to Type IV, but on several occasions a Type I pneumococcus was isolated by mouse inoculation and thus shown to be virulent.
- (4) The pneumococcus was never demonstrated in the secretion of well-cared-for children.

Briefly, therefore, the pneumococcus is to be found in the vaginal secretion of girls of the lower classes, in the type of child which frequents the Out-patient Department of a Children's Hospital, in the class of girl amongst which primary pneumococcal peritonitis occurs.

The results of this examination show that pneumococci are frequently present in the vaginal flora/

flora of low class girls, and that these pneumococci may be pathogenic. Every child therefore who harbours pathogenic pneumococci in the vagina must be regarded as a potential case of primary pneumococcal peritonitis.

If all these children could be kept properly clean, primary pneumococcal peritonitis would cease to exist.

These observations explain the "Social Incidence" of the disease, and also the immunity of well-cared-for children.

METHOD OF INFECTION OF THE VAGINA.

From a study of the clinical histories we have seen that primary pneumococcal peritonitis affects only girls of the lower classes, and at an age between 3 and 7 years.

A consideration of the foregoing facts furnishes an explanation of this. Children of the lower classes are usually not well looked after. The mother often has many children, all of which demand attention, and the housework and the preparation of meals take up a considerable amount of her time. The children are seldom washed and may only get a bath/

bath at long intervals so that their bodies and particularly the perineal region is almost invariably dirty. Their underclothing is not only dirty, but often inadequate, and insufficiently protects the lower part of the body. These children are often to be seen sitting on dirty doorsteps, pavements and common stairs. When one considers the profuse and promiscuous expectoration indulged in by the adult males of the same class, it is not surprising that some of these children become infected with the pneumococcus. Moreover children of about the ages stated above are very frequently to be seen fingering their genitals, and this further favours infection. Most of these children suffer from a certain degree of vulvitis and vaginitis, which would cause the genital tract to be a more suitable habitat for the pneumococcus.

The disease would be more likely to occur in the summer months when the children wear fewer clothes and are more out of doors, and the seasonal incidence shows this to be the case. Babies are immune because their buttocks are kept wrapped up, and it is not until they walk and go out of doors to play, that they are liable to contract the disease. Older children are less liable to contract the disease because/

because they do not sit about in the same manner as the younger children. Their clothes are longer, they do not finger their genitals to the same extent and that they spend most of their time at school. Another important fact is that older children are less susceptible to the pneumococcus than the younger ones.

Summing up, therefore, it is probable that the infection is conveyed to the vagina either by the fingers or directly from sputum.

METHOD OF SPREAD OF THE PNEUMOCOCCUS FROM THE VAGINA
TO THE PERITONEUM.

It has been shown by Bond that there is an ascending mucous current in the genital tract of the female. This observer showed that small particles of pigment placed in the vagina could later be demonstrated in the Fallopian tubes and in the peritoneal cavity. It is also recognised that gonococcal peritonitis may follow a gonococcal vaginitis, and that the organism reaches the peritoneum by way of the uterus and Fallopian tubes.

Moreover in the cases of pneumococcal peritonitis following delivery, the method of infection is by the uterus and Fallopian tubes, as pneumococci have been detected in the lochia.

Milcher/

Milcher has recently produced strong evidence that some cases of tuberculous peritonitis in the female owe their development to a genital infection. He examined a series of 14 such cases, and in 12 of them, he was able to demonstrate that the infection had extended from the internal genital organs.

It is possible, therefore, for the pneumococcus to be carried by the ascending mucous current from the vagina to the peritoneal cavity.

As the pneumococcus may commonly be found in the vaginal secretion of normal children, why should only a few be affected with the disease, and why should the disease have such a definite age incidence?

PATENCY OF THE VAGINA. Professor Arthur Robinson has suggested to me a possible explanation as to why the disease does not affect infants. At birth the walls of the vagina are in close contact and there may be a slight fusion of the two layers of epithelium due to this contact, and that the epithelial separation may not be complete until the second or third year.

I have carefully removed the vagina at a number of autopsies in young children and after hardening in bulk in either Zenker's fluid or in 10% formalin, have/

have made paraffin sections. In none of the sections examined was this fusion apparent and from a consideration of the material investigated, I think it improbable that this is the correct explanation.

THE REACTION OF THE VAGINAL SECRETION.

It is commonly taught that the reaction of the vagina is alkaline until the age of puberty and then it becomes acid. The literature on this subject is scanty and difficult to find, and there is no paper, (as far as I can find) which gives any detailed account of the reaction of the vagina from infancy to puberty. Gynaecologists lay great stress on the fact that the vagina of the adult has a definite acid reaction. This acidity is due to the action of a bacillus, Döderlein's Vagina Bacillus, which forms lactic acid, and pathogenic organisms are unable to flourish in the acid vaginal secretion.

Norris (1913) says: "At certain periods of a woman's life the secretion tends to become less acid, at times following menstruation, puerperium, and leucorrhoea, and their genital tract becomes more liable to infection."

In a personal communication, Dr Feldman informs me that all observers are now agreed that the reaction of the vagina is acid from the moment of birth onwards, although the degree of acidity varies according to the age of the infant.

Döderlein's bacillus makes its appearance within a few days of birth and the acidity increases until it reaches its maximum in the healthy adult woman.

It have tested the reaction of vaginal secretions obtained from the Out-patient Department of the Hospital, and the reaction varies. In the majority of cases it is definitely acid to litmus, but in cases where there is vaginitis and irritation it may be neutral or faintly alkaline. This suggested to me that irritation or inflammation of the vagina might be a predisposing factor in the etiology of primary pneumococcal peritonitis.

Kelly, in his "Surgical Diseases of Children", states that "Vaginitis is very common in young girls, the infection being favoured by bad hygiene, uncleanliness, scabies, thread worms and rough clothing".

Norris also calls attention to the fact that "The infrequency of vaginitis amongst adults, and its prevalence amongst little girls is most striking and can be explained by the fact that in the latter, the lining of the vagina is thin, tender, and undeveloped, and is therefore more receptive to organisms."

Moreover the "age incidence" curve in vaginitis corresponds exactly to the "age incidence" curve of primary pneumococcal peritonitis, the majority of cases/

cases occurring between the ages of 3 and 7 years.

The vaginitis is not necessarily of a severe type, but is usually a mild irritation of the lower vaginal epithelium accompanied by a slight discharge.

It is therefore probable that the reaction of the vaginal secretion is made neutral or even alkaline by reason of the vaginitis and this enables the pneumococcus to survive in the vagina.

That primary pneumococcal peritonitis occurs in young girls of the lower classes seems to be due to.-

- (1) A predisposing cause in vaginitis tending to destroy the protective acidity.
 - (2) Facilities for infection with the exciting case, the pneumococcus.
-

EXPERIMENTS ON ANIMALS.

I have shown in the foregoing pages that the historical, clinical and bacteriological evidence all favour the view that the pneumococcus reaches the peritoneum by way of the genital tract. Definite proof of this, however, is lacking. It was thought that it might be possible to produce the disease in animals by merely introducing pneumococci into the vagina, and thus prove that the genital mode of infection was possible. Moreover it was thought that information regarding the onset and course of the disease could be ascertained by such experiments.

Pneumococcal peritonitis does not exist, as far as is known, as a natural disease in any of the lower animals, but many of the laboratory animals are very susceptible to the pneumococcus, and it would seem possible to reproduce the disease in them.

ANIMALS USED. The animals used for these experiments were rabbits, rats, guinea-pigs, and later in the course of the investigation, monkeys.

White mice were used in the bacteriological examination of the clinical cases, for isolation, testing pathogenicity, /

pathogenicity, and maintaining the virulence of the strains of pneumococci examined. These experiments have been referred to in a previous section of this paper dealing with the bacteriological examination of the clinical cases.

STRAINS OF PNEUMOCOCCI USED.

- (1) Strain "STEVENS", a Type I pneumococcus which was isolated by blood culture from a fatal case of lobar pneumonia in a child.
This strain was very pathogenic. .0001 cc. of a broth culture was fatal for a white mouse in 12 hours, and .001 cc. of the culture was sufficient to kill a young rabbit in 24 hours.
- (2) Strain "GIBSON", a Type I pneumococcus which was isolated from a case of primary peritonitis in a girl aged 4 years. (Case No.7 of the present series.
Pathogenicity; .001 cc. broth culture fatal for a white mouse in 12 hours.
- (3) Strain "LOGAN", a Type II pneumococcus isolated from a case of primary pneumococcal peritonitis in a girl aged 4 years. (Case No.10 of the present series.)
Pathogenicity; .0001 cc. broth culture kills a mouse in 12 hours.

These strains were repeatedly sub-cultured at intervals of 2 days in rabbit-blood broth, and the virulence was maintained either by recovery from the experimental animal, or by passing the organisms through mice once a week, when necessary.

The material used for inoculation consisted of a 16 - 24 hours culture in nutrient broth, made according to the Rockefeller Institute technique.

The first series of experiments was intended to investigate the possibility of causing peritonitis by inoculating animals, the routes of infection being the following.

- (1) By the genital tract.
 - (2) By the blood stream.
 - (3) By the gastro-intestinal tract.
 - (4) By lymphatics.
-

EXPERIMENT I. Infection by the vaginal route.

Young female rabbits were employed. They were held by an assistant, and a very small red rubber catheter moistened with saline carefully introduced into the vaginal cavity, especial care being taken to avoid damage to the mucous membrane. Pneumococci were then introduced along the catheter.

The following is a protocol of such an experiment.

Rabbit P. 6. Young female, weight 1130 grams.

1.3.21. 4.30 p.m. .5 cc. broth culture of pneumococci "Stevens" introduced in vagina.

3.3.21. 9 a.m. Animal found dead. Autopsy revealed no peritonitis but an intense septicaemia, very numerous capsulated cocci being found in the blood stream. The vagina and uterus were inflamed but no pus was observed.

This series of experiments shows that when pneumococci are introduced into the vagina of young rabbits, the animals die of septicaemia before the organism has had time to reach the peritoneal cavity.

As the animal in such an experiment may die in/

in 24 hours from an intense septicaemia, without apparent injury of the vaginal mucous membrane, experiments were done to find out when the pneumococcus enters the blood stream after such an infection.

Blood was withdrawn from the ear vein, measured by means of a syringe and then added to melted agar at 50°C, and poured into Petri dishes. The number of colonies present after incubation was noted and the number of organisms per cubic centimetre of blood calculated.

The following is the protocol of a typical experiment.

EXPERIMENT II.

Rabbit P. 8. A young female, weight 830 grams.

3.3.21. 5 p.m. .5 cc. culture of pneumococci
"Stevens" in vagina. Temperature 102.4°F.

4.3.21. 10 a.m. .5 cc. blood withdrawn; colonies
2000 per cc. Temperature 104.4°F.

4.3.21. 5 p.m. .5 cc. blood withdrawn; colonies
innumerable. Temperature 106°F.

5.3.21. 9 a.m. Animal found dead.
Autopsy showed an intense septicaemia,
no peritonitis. Vagina, uterus and
Fallopian tubes were much inflamed.

This experiment shows that a very heavy infection of the blood stream may occur as soon as 17 hours after the introduction of pneumococci into the vagina.

Sometimes, in spite of a very heavy infection with the pneumococcus, the rabbit recovered. This was noticed in older rabbits, as the following protocol shows.

EXPERIMENT III.

Rabbit P. 10. Old female, weight 1675 grams.

- | | | |
|----------|-----------|---|
| 3.3.21. | 4.15 p.m. | .5 cc. broth culture of pneumococci, "Stevens" introduced into vagina. |
| 4.3.21. | 5 p.m. | .5 cc. blood withdrawn; colonies 7000 per cc. |
| 6.3.21. | 2 p.m. | Animal still alive; .4 cc. blood withdrawn. Colonies - nil. |
| 9.3.21. | - | Animal alive and well. .5 cc. blood withdrawn. Colonies - nil. |
| 10.3.21. | - | Animal killed. No peritonitis, culture from heart blood sterile. Uterus and vagina appear congested. Culture from uterus was sterile. |

This experiment is instructive in showing that a susceptible animal such as the rabbit, may overcome a heavy pneumococcal infection of the blood stream.

As young rabbits are too susceptible to the pneumococcus, experiments were made using old animals with less virulent cultures; and also by immunising the animal against the pneumococcus before infection.

Determinations were made on the blood chlorides, as it is well known that blood chlorides are reduced in pneumococcal infections, and it was thought that information as to when this reduction occurred, and also the fate of the blood chlorides might be ascertained.

EXPERIMENT IV. Inoculation of an old animal with a less virulent culture.

Pneumococcus, strain "Stevens", was sub-cultured on serum-agar slopes at 3 day intervals for 14 days in order to reduce the virulence. A broth culture was used for inoculation.

This series of experiments failed to cause peritonitis or death of the animal.

Protocol./

Protocol.

Rabbit. P. 16. An old female, weight 2010 grams.

22.4.21. Temperature 102.4°F.

25.4.21. .5 cc. broth culture pneumococci "Stevens"
(attenuated) in vagina.

28.4.21. Animal had remained alive and well.
Temperature 102.4°F. .5 cc. blood with-
drawn. Colonies - nil.

30.4.21. Animal alive and well. .5 cc. blood
withdrawn. Colonies - nil.

1.5.21. .5 cc. broth culture pneumococci "Stevens"
(attenuated) in vagina.

2.5.21. .5 cc. blood withdrawn. One colony de-
veloped. Temperature 102.6°F.

3.5.21. .5 cc. blood withdrawn. Colonies nil.
Temperature 102.4°F.

6.5.21. Animal alive and well.

EXPERIMENT V. In this series, animals were first immunised by three doses of killed pneumococci, given at intervals of 5 days. They were then inoculated in the vagina with virulent pneumococci. In only one case did peritonitis occur, and that only consisted of a layer of fibrin over the fimbriae of the tubes. The other animals either died of pneumococcal septicaemia or failed to be infected.

Protocol.

Rabbit P. 19. A young female, weight 1095 grams.

- 20.4.21. .5 cc. killed culture of pneumococci
"Stevens" subcutaneously.
- 25.4.21. 1 cc. killed culture subcutaneously.
- 30.4.21. 1.5 cc. killed culture intraperitoneally.
- 5.5.21. Inoculation in vagina with .5 cc. broth
culture of virulent pneumococci "Stevens".
- 6.5.21. Animal appears unwell.
- 7.5.21. Animal found dead.

Autopsy shows a layer of greenish fibrin over the fimbriae of the Fallopian tubes. Uterus and tubes congested. No general peritonitis. The Blood film shows numerous capsulated diplococci.

From these foregoing experiments it was obvious that it would be impossible to reproduce the clinical disease in rabbits. These animals are unfit for the purpose for two reasons.

- (1) They are too susceptible to the pneumococcus.
- (2) The uterus and Fallopian tubes are too long, too narrow and too tortuous. The animal dies of septicaemia long before the infection reaches the peritoneum.

However studies on absorption of organisms from the peritoneal cavity, and a study of blood chlorides could be undertaken in these animals.

EXPERIMENT VI. Jensen showed that when pneumococci were injected into the peritoneal cavity of the guinea pig, organisms could be demonstrated in the blood stream within a few minutes of injection. This experiment was repeated on a number of rabbits and Jensen's results confirmed. The time that organisms appeared in the blood stream varied from 4 to 10 minutes after intra-peritoneal injection, the time depending on the number of organisms injected and also on the age of the rabbit. Samples of blood, 0.5 cc. in amount were withdrawn from/

from the ear vein at various intervals after intraperitoneal injection. These samples were mixed with agar at 50°C, in Petri dishes and the number of colonies developing were counted after 48 hours incubation.

The average time for organisms to appear in the circulation was 6 minutes after intraperitoneal injection.

Protocol.

Rabbit P. 26. Male. Weight 1958 grams.

26.6.21.

11.10 a.m.	5 cc. broth culture pneumococci			
	"Stevens" inoculated intra-			
	peritoneally.			
11.14 a.m.	.5 cc. blood withdrawn.	Colonies		0
11.16 a.m.	.5 cc. " "	" "	" "	1
11.23 a.m.	" "	" "	" "	7
11.30 a.m.	" "	" "	" "	88
11.40 a.m.	" "	" "	" "	138
11.55 a.m.	" "	" "	" "	285
12.12 p.m.	" "	" "	" "	469
12.40 p.m.	" "	" "	" "	1300

22.6.21.

11.30 a.m. Animal died with a profound septicaemia.
Autopsy revealed no peritonitis.

This/

This experiment is interesting because it shows that the peritoneum is much more resistant to infection by the pneumococcus than the blood stream.

EXPERIMENTS ON BLOOD CHLORIDES.

It has long been known that in pneumococcal infections, the chlorides excreted in the urine are much diminished. Determinations of the blood chlorides are also stated to be reduced in amount. It was thought that determinations of the blood chlorides during a pneumococcal infection of the rabbit might throw some light on the human phenomenon.

Bang's method of determining blood chlorides was employed according to the technique given in Cole's "Practical Physiological Chemistry".

The method briefly is as follows:-

A small stoppered bottle containing a strip of filter paper is carefully weighed. The ear vein of the rabbit is pricked and a drop of blood is absorbed by the filter paper. The bottle is then reweighed, the increase being the weight of blood. 10 ccs. of acid magnesium sulphate solution are now measured into a test tube and boiled. Into this boiling fluid, the strip of filter paper containing the blood is now dropped. This causes the proteins in the blood to be/

be coagulated and also the chlorides to go into solution. The fluid is now cooled, and 2 ccs. of N/100 silver nitrate solution are added. This causes a precipitation of all the chlorides as silver chloride, the amount of silver nitrate solution being in excess. The contents of the tube are filtered through kieselguhr in a Gooch crucible. The filtrate contains the excess of silver nitrate not required to precipitate the blood chlorides. To the filtrate are added 2 ccs. of potassium iodide-iodate solution and a little starch solution. The fluid is now blue owing to the action of the iodate on the starch solution. The standard silver nitrate solution is now carefully run in with a micro-burette until the blue colour is just discharged. The reading gives the amount of silver nitrate solution required to precipitate the blood chlorides.

The explanation of the technique is as follows.

1 cc. of silver nitrate solution is exactly neutralised by 1 cc. of the potassium iodine iodate solution. 2 ccs. of silver nitrate solution are added to the fluid which contains the blood chlorides. The filtrate contains the amount of silver nitrate solution which is in excess of the amount required to precipitate the chlorides. To this is added 2 ccs. of/

of potassium iodine iodate solution. If all the silver nitrate added had come through the filter, then the 2 cc. added would have exactly neutralised the 2 cc. of iodine iodate solution, but some silver nitrate was used to precipitate the blood chlorides, so therefore less than 2 ccs. come through the filter and this is not sufficient to neutralise all the iodine-iodate solution added. Silver nitrate solution therefore is run in from a micro-burette until the iodine-iodate solution is just neutralised and this amount is equivalent to the amount of N/100 silver nitrate solution required to precipitate the blood chlorides. 1 cc. N/100 silver nitrate solution is equivalent to .000585 gram of sodium chloride.

Knowing the weight of blood taken, the blood chlorides are estimated as the percentage of sodium chloride. Controls however are necessary. Firstly the micro-burette has to be standardised by filling it with mercury and weighing out the successive quantities of mercury run off. A curve is then constructed from these data with the actual reading on one abscissa and the corrected reading on the other abscissa so that any reading may be easily corrected. Secondly the kieselguhr absorbs a little silver nitrate, this must be determined for the amount of/
of/

of kieselguhr used.

The following is a protocol of a typical determination.-

Weight of bottle - filter paper	7.0328 grams.
Weight of bottle - filter paper	
- blood	<u>7.1687 "</u>
Weight of blood	.1359 grams.

Burette reading 1.27 cc. Corrected 1.197 cc.

Silver solution absorbed by
kieselguhr = .03 cc.

$$\text{NaCl \%} = \frac{100 \times 1.167 \times .000585}{.135}$$

$$= .5057\% \text{ NaCl.}$$

If care is taken during the titration, this method gives good results.

In the following experiment the rabbit received 1 cc. of a broth culture of virulent pneumococci intraperitoneally. Samples of blood were withdrawn at intervals and the chloride content determined.

EXPERIMENT VII.

Rabbit P. 28. Female, weight 1130 grams.

22.6.21.

11 a.m.	Blood chlorides estimated	.538%
11.10 a.m.	1 cc. broth culture of pneumococci "Stevens" intraperitoneally.	
11.18 a.m.	Blood chlorides estimated	.528%
11.33 a.m.	" " "	.530%
12.12 p.m.	" " "	.533%
2.27 p.m.	" " "	.529%
5.30 p.m.	" " "	.536%

23.6.21.

11 a.m.	" " "	.533%
11.45 a.m.	rabbit died from septicaemia.	

The amount of variation in the percentage of blood chlorides is very small and is well within the limits of experimental error.

The above experiment shows that during a rapid pneumococcal infection (24 hours) there is no diminution in blood chlorides.

Similar experiments were done, the rabbit receiving pneumococci intra-vaginally, but in no case was there any reduction in the blood chlorides.

Pneumococci/

Pneumococci introduced intravenously into rabbits also had no effect in reducing blood chlorides.

The rabbit therefore is unsuitable for the study of the fate of blood chlorides, because the animal dies of septicaemia before the alteration, if any, takes place.

EXPERIMENTS ON THE TRANSMISSION OF PNEUMOCOCCI TO THE PERITONEUM FROM THE VAGINA BY LYMPHATICS.

It has been suggested by some observers that pneumococci might reach the peritoneum from the vagina, not by the uterus and tubes, but by lymphatics. In the following series of experiments, the vagina of the rabbit was scarified, and a small quantity of pneumococcus culture introduced. A severe vaginitis with subcutaneous abscesses and also cystitis usually developed, but in no case was there any evidence of spread to the peritoneum.

Protocol./

Protocol.EXPERIMENT VIII.

Rabbit P. 30. A young female, weight 1220 grams.

		Temper- ature.	Chlor- ides.	Colon- ies.
29.6.21.	Vagina scarified, .05 cc. of a broth culture of pneumococci "Stevens" inocu- lated on Scari- fication.	102.4°F.	.504%	-
30.6.21.	.5 cc. blood withdrawn	105.0°F.	.5067%	105.
1.7.21.	.5 cc. blood withdrawn	105.6°F.	.5182%	5200.
	The vagina is swollen and con- gested and there is a severe vaginitis.			
3.7.21.	Animal died	106.2°F.	.508%	Count- less.

The autopsy revealed no peritonitis, but a severe vaginitis, with subcutaneous abscesses round the vagina. There was a marked cystitis. Death was due to septicaemia.

This series of experiments is interesting. Firstly, there is no evidence of spread of organisms from the vagina to the peritoneum by lymphatics, and secondly, after 5 days infection, there was no reduction of blood chlorides.

EXPERIMENTS ON FEEDING WITH PNEUMOCOCCI.

Jensen, (see page 19) fed guinea pigs with pneumococci and on one occasion had caused a severe enteritis, with necrosis of the Peyer's patches through which the pneumococci had passed into the peritoneal cavity just before the fatal termination.

These experiments were repeated, but using rabbits instead of guinea pigs, to ascertain if it was possible to cause a true peritonitis by introducing organisms into the alimentary canal.

A culture of pneumococcus was introduced into the stomach by means of a catheter. This is a very simple procedure if the animal is suspended by the lower jaws in a special box. This method of feeding was shown to me by Dr J.W. McNee, who had used it in Professor Aschoff's laboratory in Freiburg. It is first necessary to fast the animal for 24 hours, otherwise the introduction of fluid into a full stomach will cause over-distension and death.

10 ccs. of virulent pneumococci grown in rabbit blood broth were introduced, this constituting a very large dose.

A series of rabbits were fed with virulent pneumococci only.

Protocol.EXPERIMENT IX.

Rabbit P. 33. Male, weight 1530 grams.

23.8.21. 10 ccs. rabbit-blood broth culture of pneumococci "Gibson" introduced into the stomach. Temp. 102.4°F .

24.8.21. Animal alive and well. Temperature normal (102.4°F .).

26.8.21. Animal alive and well. No diarrhoea. Temperature normal. The animal continued alive and well.

This series of experiments showed that it was impossible to produce any gastro-intestinal disturbance, even with large doses of virulent pneumococci.

There was always the possibility that the pneumococci were killed off by the gastric juice before gaining entrance to the intestine.

A similar series of experiments was done, but the gastric juice was neutralised previously with sodium bicarbonate.

Protocol./

Protocol.EXPERIMENT X.

Rabbit P. 38. Female, weight 1710 grams.

Animal fasted 24 hours.

27.8.21. .6 grams of sodium bicarbonate in 10 cc. of water introduced into the stomach.

10 minutes later 10 cc. rabbit blood broth culture of Pneumococci "Gibson" introduced.

28.8.21. Animal alive and well, temperature normal.

Animal remained alive and well.

This series of experiments shows that even when the gastric juice is neutralised, no gastro-intestinal disturbances are caused by large doses of pneumococci.

In the next series of experiments, the gastric juice was neutralised, and in addition, the peristaltic movements of the intestine were inhibited with tincture of opium. It was thought that the absence of intestinal movement might permit of the passage of the pneumococcus through the intestinal wall. The following is a protocol of such an experiment.

EXPERIMENT XI./

EXPERIMENT XI.

Rabbit P. 42. Male, weight 1950 grams.

30.8.21. .6 gram sodium bicarbonate and .3 cc. Tinct. Opii in 10 ccs. of water were introduced into the stomach. 15 minutes later 10 ccs. rabbit-blood broth culture of pneumococci "Gibson" introduced.

31.8.21. Animal alive and well and remained so for a week when the animal was returned to stock.

These series of feeding experiments show that virulent pneumococci introduced into the gastro-intestinal canal of such a susceptible animal as the rabbit, exert no pathogenic effects.

These experiments entirely negative the theory of infection of the peritoneum from the intestinal canal in cases of primary pneumococcal peritonitis.

As the rabbit is unsuitable for the production of pneumococcal peritonitis by vaginal inoculation, it was decided to try the experiments on rats and guinea pigs.

A few young animals of both species were used, but no peritonitis could be produced. The long uterus/

uterus and tubes prevents the pneumococcus from gaining access to the peritoneal cavity. It was decided therefore to continue these experiments, using young female monkeys for the purpose.

Monkeys are particularly suitable for such experiments because:-

- (1) Their susceptibility to the pneumococcus is about equal to that of the child.
- (2) The anatomical arrangement of the internal genital organs are similar to, and comparable with those of the human being.

It was obvious that to reproduce the clinical picture of the disease as met with in children it would be necessary to obtain young female monkeys. This was more difficult than it was thought to be and after waiting for 6 months, three suitable animals were obtained.

Pneumococci were introduced into the vagina by means of a soft red rubber catheter. About .5 cc. of a broth culture was used for inoculation.

EXPERIMENT XII.

Monkey P. 1. Young female Bonnet Monkey.

12.12.21. Inoculated in vagina with .5 cc. broth culture of pneumococci "Gibson".

22.12.21./

22.12.21. Animal remained alive and well up to this date. During the Christmas vacation, the monkey became listless and later commenced a spastic paralysis in the hind legs.

7.1.22. Monkey died.

Autopsy showed remains of an old peritonitis. Some of the coils of intestine were adherent. There was no pus formation, and no pneumococci could be obtained on culture from the peritoneal cavity.

This experiment is a doubtful one. The post-mortem findings would indicate that a very mild form of peritonitis occurred, from which the monkey recovered. No pneumococci could be recovered from the peritoneal cavity, but this observation would be expected if the animal had recovered from a peritonitis.⁵

The exact cause of death of the animal was not ascertained.

Although I draw no conclusions from this experiment, I think it is probable that a mild chronic peritonitis occurred and the animal recovered. This would indicate that it was possible to cause pneumococcal peritonitis by simple intra-vaginal inoculation with the pneumococcus.

EXPERIMENT XIII.

Monkey P. 2. Young female Macacus Rhesus.

- 14.1.22. Monkey inoculated in vagina with .5 cc. culture of pneumococcus "Logan".
- 17.1.22. Animal remained alive and well.
- 21.1.22. Animal had remained alive and well up to this date. Inoculated again in vagina with .5 cc. culture of pneumococcus "Logan".
- 12.2.22. Animal remained alive and well up to this date. Vagina washed out with a dilute solution of sodium bicarbonate, then 1 cc. of a blood broth culture of pneumococci Logan introduced.
- 14.2.22. Animal unwell, not feeding, sits quiet in the cage holding its abdomen.
- 15.2.22. Monkey still unwell, not eating its food. Animal tries to lie with its abdomen on the hot pipes.
- 16.2.22. The animal is unwell but appears slightly better.
- 17.2.22. The animal is a little better. The monkey was killed on this date by chloroform.

Autopsy revealed a generalised peritonitis which was more severe in the pelvis than in the upper part of the abdomen. The intestines were matted together with greenish-yellow pus. In films from the pus, capsulated diplococci were present, and from cultures, a Type II pneumococcus was obtained.

The uterus, Fallopian tubes showed nothing abnormal on naked-eye examination. Cultures from the Fallopian tubes gave a very scanty growth of Pneumococcus Type II.

The whole genital tract was removed en masse and fixed in Zenker's fluid.

Sections showed no inflammation in the vagina.

The uterine mucous membrane is normal, but in the cavity of the uterus there is a little fibrin and a few pus cells. From the absence of any inflammatory reaction in the mucous membrane I am of the opinion that this fibrin was due to haemorrhage into the cavity of the uterus caused by removing the genital tract immediately after death when the blood was still fluid.

The mucous membrane of the Fallopian tubes is normal, as may be seen from the accompanying micro-photographs.

This experiment shows that inoculation in the vagina/

vagina causes a typical primary pneumococcal peritonitis in monkeys and that there is no inflammatory reaction caused by the passage of the pneumococcus along the genital tract.

DISCUSSION OF THE RESULTS OF THE EXPERIMENTS
ON ANIMALS.

The rabbit is unsuitable for experiments for proving the genital theory of infection of primary pneumococcal peritonitis, because of its susceptibility to the pneumococcus and also because of the anatomical arrangement of its internal genital organs. Several interesting facts however are elicited from these experiments.

Firstly, that the pneumococcus can get through an uninjured mucous surface.

Secondly, that a rabbit may recover from a heavy infection of the blood by the pneumococcus.

Thirdly, that pneumococci can gain entrance to the blood stream very easily from the peritoneal cavity, and organisms may be demonstrated in the blood stream 4 minutes after intraperitoneal injection.

Fourthly./

Fourthly. There is no reduction in the blood chlorides in pneumococcal infections in the rabbit.

The view that the infection is blood borne because even in the earliest stages of the disease pneumococci can be found in the blood stream, is disproved by these experiments. In the rabbit it only takes 4 minutes for pneumococci to get from the peritoneum to the blood stream, and probably in human cases the time would not be much longer. Very few cases are seen and diagnosed within 12 hours of the onset of the disease and by that time very numerous organisms have gained access to the blood stream from the peritoneal cavity.

The feeding experiments are interesting. It was impossible to cause any gastro-intestinal disturbances in rabbits even after massive doses of virulent pneumococci. Even when conditions were most favourable, when the gastric juice was neutralised, and the intestinal movements were slowed, there was no evidence of any pathogenic effects of a virulent organism on a very susceptible animal. It is therefore most unlikely that the pneumococcus can get through/

through the healthy mucous membrane in a person in good health and without any previous gastro-intestinal symptoms.

I consider that these experiments disprove conclusively the intestinal theory of infection.

The experiments on monkeys show that infection of the peritoneum by way of the genital tract is possible. In one monkey the clinical picture of the disease was produced after vaginal inoculation, and this shows that it is possible for the pneumococcus to ascend the genital tract and cause infection of the peritoneum. The experiment itself is very interesting. Two simple inoculations failed to reproduce the disease. After washing out the vagina with dilute alkali, infection of the peritoneum was possible. Was this due to the neutralising of the normal acid reaction of the vagina, or was it due to the mucus being dissolved away by the alkali?

The main point proved is that the genital mode of infection is possible and that a neutral or alkaline reaction of the vagina favours such an infection.

Another interesting point is the absence of any lesions in the Fallopian tubes, although the pneumococcus was cultivated from them, showing that the pneumococcus/

pneumococcus does not cause any pathogenic effect during its course along the genital tract and that it is only when the organism reaches the peritoneal cavity that it gives rise to disease.

CONCLUSION AND SUMMARY.

In this investigation I have discussed the possible means of infection of the peritoneum in primary pneumococcal peritonitis. Three theories are worth considering - (1) that the infection reaches the peritoneum by the blood stream; (2) that it is due to extension from the intestines; and (3) that it gains access to the peritoneum from the exterior by the genital tract. I have endeavoured to show that the last theory is the correct one.

The main points of evidence against the first theory, that the infection comes from the blood stream, are:-

- (1) Sex, age, seasonal and social incidence.
- (2) Absence of focus of pneumococcal infection (in primary cases).
- (3) The extreme rarity of the disease in cases in which we know that pneumococci are circulating in the blood stream (e.g. in pneumonia).
- (4) Animal experiments show that the intravenous injection of pneumococci never causes peritonitis.

The/

The main points of evidence against the second theory, that the infection comes from the intestinal canal, are:-

- (1) Sex, age, seasonal and social incidence as above.
- (2) The sudden onset of the disease without previous gastro-intestinal disturbances.
- (3) At the autopsy of cases of primary pneumococcal peritonitis, the intestinal tract is found to be normal.
- (4) In pneumonia, where abundant virulent pneumococci are swallowed, and gastro-intestinal disturbances are frequent, peritonitis is one of the rarest complications.
- (5) The disease has never been reproduced by feeding animals with pneumococci.

The following facts which have been obtained during the course of this investigation all support the third theory, that the infection gains entrance to the peritoneum by the genital tract.

- (1) The disease occurs only in girls; boys are immune.
- (2) The majority of cases occur between the ages of 3 and 8 years; infants and adults scarcely ever contract primary pneumococcal peritonitis.
- (3)/

- (3) Unlike pneumonia, the disease occurs most frequently in the summer months.
- (4) The girls attacked by the disease belong to the lower classes.
- (5) Such children frequently suffer from vulvo-vaginitis, and in them the vaginal secretion may be neutral or alkaline in reaction, thus permitting the growth of the pneumococcus.
- (6) Virulent pneumococci can be isolated from the vaginal secretion of healthy girls of the lower classes.
- (7) The infection may be carried to the vagina by the fingers, or there may be direct infection from sputum-contaminated dust.
- (8) The disease occurs suddenly in healthy children and the first symptom is sub-umbilical pain.
- (9) At laparotomy, it can be shown that the disease begins in the pelvis, and in early cases it is confined to the lower abdomen.
- (10) Pneumococci have been found in the vagina in all cases of the disease examined, and these pneumococci are always of the same Type as that causing the disease.

- (11) The pneumococci in the throat may be of the same Type as those found in the peritoneum. But in one case they were of a different type, thus showing that the path of entrance of the infection was neither the pharynx nor the intestinal canal.
- (12) At autopsy the peritonitis is the only lesion present. There is no sign of any gastrointestinal lesion which would permit of the entrance of pneumococci to the peritoneum. and
- (13) The disease can be reproduced in monkeys by the inoculation of the vagina with pneumococci. The organisms ascend the genital tract and do not cause symptoms until they reach the peritoneal cavity.

I therefore consider that I have shown that Primary Pneumococcal Peritonitis is a disease which affects females only, and that the infection reaches the peritoneum by way of the genital tract.

ADDENDUM.

Since writing the above I have had access to a paper recently published by Koennecke. (Beit. zur klin. Chir. 1919, Bd 115).

In discussing the etiology of primary pneumococcal peritonitis, Koennecke, on clinical grounds does not think that the infection of the peritoneum is by the blood stream. He considers that the genital path of infection is the probable one as the preponderance of cases are in girls (he does not distinguish between "primary" and "secondary" cases), and that the infection usually begins in the pelvis. Koennecke further states: "One must not forget that pneumococcal peritonitis in relation to other pneumococcal infections, especially pneumonia, is extraordinarily rare. Further the female genital organs have never been systematically examined for pneumococci in pneumococcal peritonitis. Difficulties must stand in the way of such a research. Post-mortem examinations in such cases are not free from objection, and in the living subject practically the only consideration is that of the vaginal secretion, in which pneumococci are easily missed (in films), or, on account of their delicacy, are easily overgrown by other/

other organisms. The question now is, how do pneumococci get into the female genitals?"

Koennecke thinks that infection is from the faeces, the organisms first getting into the mouth and then passing to the intestinal canal.

(Case No.4 of the present series, in which the pneumococcus found in the mouth was of a different Type from the one causing the peritonitis, disposes of this theory).

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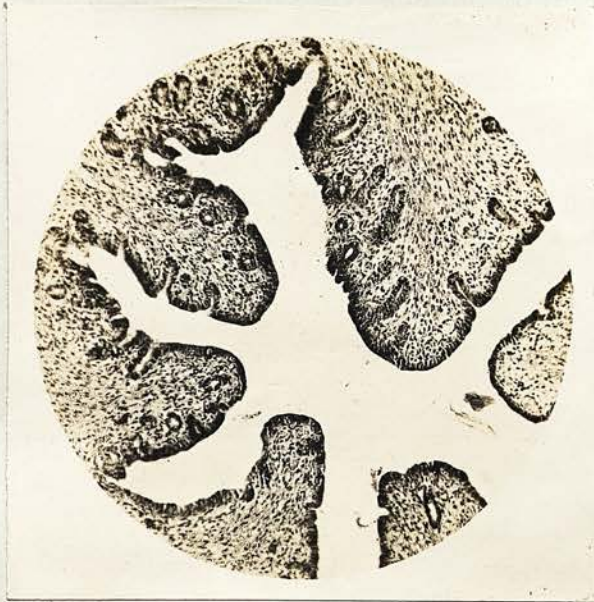
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RABBIT P. 6. SECTION OF VAGINA.

Leitz apochromat 16 mm. eyepiece 2.

The rabbit died of septicaemia
after intra-vaginal inoculation
with pneumococci. There is no
inflammatory reaction.



RABBIT P. 6. SECTION OF FALLOPIAN TUBE.

Leitz 16 mm. apochromat. eyepiece 2.

The mucous membrane shows no evidence of inflammation.



RABBIT P. 6. SECTION OF UTERUS.

Leitz 16 mm. apochromat. eyepiece No.2.

The rabbit died of Septicaemia after vaginal inoculation with pneumococci.

The mucous membrane is normal. There is no evidence of inflammation.



CASE No.5. SECTION OF VAGINA.

Leitz apochromat. 16 mm. eye-
piece 2.

There is a slight vaginitis
with desquamation of the
epithelial cells.



CASE No.5. SECTION OF VAGINA.

Zeiss 8 mm. apochromat. eye-
piece 2.

There is a definite vaginitis
present with desquamation of
epithelial cells.



CASE No.5. SECTION OF UTERUS.

Leitz 16 mm. apochromat. eye-
piece 5.

The mucous membrane lining the
uterus shows no evidence of
inflammation.



CASE No.5. FALLOPIAN TUBE.

Leitz 16 mm. apochromat.

eyepiece 2.

The mucous membrane is normal.



CASE No.5. SECTION OF BROAD LIGAMENT.

Leitz 16 mm. apochromat. Eyepiece No.2.

Note the extreme congestion of the
bloodvessels.



CASE No.8. SECTION OF UTERUS.

Zeiss 8 mm. apochromat. eye-piece 2.

There is no evidence of inflammatory reaction in the uterus although the pneumococcus travelled through it to the peritoneum.



CASE No.8. SECTION OF FALLOPIAN TUBE.

Leitz apochromat 16 mm. eyepiece 2.

There is an acute inflammation on the peritoneal surface of the tube.

The mucous membrane is normal and shows no evidence of inflammation.



CASE No.8. SECTION OF FALLOPIAN TUBE.

Zeiss 8 mm. apochromat. eyepiece 2.

The mucous membrane is normal and
shows no evidence of inflammation.



MONKEY P. 2. SECTION OF VAGINA.

Leitz 16 mm. apochromat. eye-
piece 2.

A slight amount of vaginitis
present.



MONKEY P. 2. SECTION OF VAGINA.

Zeiss 8 mm. apochromat. eyepiece 2.

There is evidence of slight vaginitis, but the epithelial surface is practically normal.



MONKEY P. 2. SECTION OF UTERUS.

Zeiss 8 mm. apochromat. Note
slight amount of red blood
corpuscles and fibrin.



MONKEY P. 2.

SECTION OF FALLOPIAN TUBE (left).

Zeiss 8 mm. apochromat. eyepiece 2.

The mucous membrane is normal and
shows no evidence of inflammation.



MONKEY P. 2.

SECTION OF FALLOPIAN TUBE. (right)

Zeiss 8 mm. apochromat. eyepiece 2.

The mucous membrane is normal.